The Journal of
Obstetrics & Gynaecology
of the British Empire

VOL. 43, No. 6 NEW SERIES DECEMBER, 1936

Further Observations on the Relation of Pregnancy to Hypertension and Chronic Nephritis.

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THE view is widely held, both in this country and in the United States of America, that chronic nephritis may occur *de novo* during and solely as the result of pregnancy. Indeed, many authors infer that the indirect mortality associated with childbirth and resulting from chronic nephritis is greater than the mortality associated with parturition. The term nephritis is used loosely, and includes those cases of renal failure due to arterio-sclerotic changes in the kidneys, and it will be so used in this paper. This view is based mainly on two facts: (1) That toxaemic albuminuria frequently recurs in subsequent pregnancies; (2) that women die from renal failure subsequent to suffering from the toxaemic albuminuria of pregnancy, although renal symptoms were not detected when these women first attended the antenatal clinics.

If there were a marked causal relation between pregnancy and chronic nephritis it would be reasonable to suppose that the mortality rates for the latter condition would be higher in women than in men. This is not the case, for in every district in England and Wales, and during every decade since vital statistics

were first collected, the mortality rates for this disease for men have exceeded those for women (Theobald).[4] I further showed that there was not any evidence of an additional causal factor operating during the childbearing period, and there was no significant difference between the mortality rates for chronic nephritis for married and single women up to the age of 55 years. These and other relevant conclusions were drawn from a report dealing with an estimated mean population of 19,238,700 females for the decade 1911–1922. The argument that deaths from nephritis might have been classified in other categories was met by a study of the mortality rates for cerebral thrombosis and haemorrhage, and circulatory failure which in no way invalidated the main conclusions. Deaths from renal and circulatory failure and cerebral haemorrhage are probably the most accurately certified of all causes of death, and the single fact that the mortality rates from Bright's disease in women have followed the same upward and downward tendencies as those for men, whatever area of the country is investigated, makes it reasonably certain that the conclusions are not invalidated because of inaccuracy of certification. It must, therefore, be concluded that the facts on which the orthodox view is based must be capable of a different interpretation. The purpose of this paper is to offer evidence in favour of the view that the chronic nephritis precedes but does not result from the pregnancy. It is proposed briefly to discuss (*a*) albuminuria, (*b*) hypertension, (*c*) the hereditary or familial factor associated with chronic nephritis, (*d*) certain cases illustrating specific points.

It is, however, essential at the outset to make two assertions which are of fundamental importance: (*a*) That a woman known to pass albumin constantly in the urine may pass a protein-free urine during the first half of pregnancy; (*b*) that the blood-pressure of a woman known to suffer from hypertension may fall to the normal level during the early months of her pregnancy. The assumption that a woman who passes an albumin-free urine and has a normal blood-pressure when she first attends an antenatal clinic is healthy and not suffering from renal disease may, therefore, not be warranted.

Albuminuria.

It is proposed to consider albuminuria more fully elsewhere, but there are certain facts which are pertinent to the present subject. I have reported (Theobald[3]) that albumin was present in the urines of 23.6 per cent of 110 college girls, in 16.7

per cent of 5,042 girls of the age of 14, and in 8.2 per cent of 912 charwomen over the age of 25 years. It was further reported that only 10 out of 22 women medical students consistently passed urines either free from or containing less than a trace of albumin. On the other hand, it is well known that less than 1 per cent of women attending an antenatal clinic pass albumin in the urine during the first six months of pregnancy. It cannot be maintained that the results reported in 1932 are invalid because the urines were passed naturally, for pregnant women of the hospital class are much more likely to pass contaminated urines than college girls. I have, moreover, drawn attention to the fact that women known to suffer from albuminuria secrete albumin-free urine during the first half of pregnancy (Theobald).[3, 5] [Such a patient is at present in the ward as this paper is being written.] Of 795 patients who made two or more attendances at the antenatal clinic at St. Mary Abbot's Hospital during 1935 only eight passed albumin in the urine at any time during pregnancy. The amount of albumin passed, except during labour, was not in any case more than 0.05 per cent, while in four of these women the albuminuria cleared up completely within three days of admission and some time before labour commenced. Of the remaining four patients at least three suffered from undoubted chronic glomerulo-nephritis.

I have shown that a relatively slight increase in pressure in the renal veins is sufficient to cause albuminuria in animals and in man, although the amount of albumin present in the urine as the result of this insult varies from individual to individual, and is probably in part dependent on the permeability of the glomerular tufts (Theobald).[2] Kerridge and Bayliss, and Kerridge, primarily concerned with investigating whether the kidneys were able selectively to excrete abnormal proteins, concluded that the renal glomeruli function as graded filters permitting molecules smaller than serum albumin to pass, and withholding all others. This view, in accord with that which explains why protein may appear in the urine after the injection of egg albumin, fails to explain the ready passage of haemoglobin, which has approximately the same molecular weight as serum albumin. It, moreover, fails to explain why in the majority of cases of orthostatic albuminuria the protein in the urine consists largely of globulin which has a much higher molecular weight than serum albumin, and is present in much smaller amounts in the blood-plasma. For the past three years I have been subjecting the urines of women suffering from pregnancy albuminuria to ultrafiltration,

and it is clear that the proteins of such urines pass through collodion membranes with the same or greater ease than egg albumin. An artificial is not a living membrane, and the interpretation of these results is beset with many difficulties. It will suffice at the present to say that the passage of a protein through such a filter is dependent on a number of factors, including the following: the electrical charges possessed by the molecules and the viscosity, surface tension and presence of other substances in the fluid being filtered. If a protein in solution is unable to pass through such a membrane it may happen that the addition of a further protein to the solution will result in the passage of both proteins through the filter. Utrafiltration is not comparable with sieve action. Sørensen has advanced the view that the plasma proteins are not stable chemical entities. He regards them as being made up of stable main valency units, probably polypeptides, which are loosely held together by residual valencies. In other words, serum albumin, as we know it is only serum albumin under certain specific physico-chemical conditions. McFarlane, using the ultracentrifuge has obtained results which for the most part are consistent with the views of Sørensen. In this, the first attempt to use the ultracentrifuge for the purpose, he has shown that significant changes occur in the serum protein in disease, and that there are differences between the urinary and serum proteins. It may be that the heteroproteins of McFarlane support Sørensen's thesis, or it may be that their presence makes it possible for the normal proteins to pass through the glomerular tufts (on the analogy of the collodion membranes). The thesis I wish to advance is that the severe and sudden onset of albuminuria during pregnancy may be due to changes in the blood-plasma and that the condition may occur apart from either functional or structural changes in the kidneys. This extra-renal conception of the albuminuria of pregnancy, and probably of nephrosis, would make the condition strictly analogous to the glycosuria of diabetes. This view is consistent with the following facts: (*a*) That albuminuria is but rarely encountered in patients less than 26 weeks pregnant, and that if albumin is normally present in the urine it tends to disappear during the first six months of pregnancy. (*b*) That the albuminuria of pregnancy may be almost entirely prevented and cured if discovered at an early date simply by placing the patient on a diet rich in proteins, minerals and vitamins. (*c*) That the onset of a severe degree of albuminuria may be very rapid and unaccompanied by any evidence of impairment of renal function. (*d*) That signifi-

cant histological changes are usually absent in the kidneys of women dying from eclampsia.

A brief note concerning one patient will serve to illustrate this conception.

> N.L., aged 31 years, a primigravida with a history of scarlet fever, was admitted with hypertension without albuminuria. Her blood-pressure fell to 136/82 mm. Hg. She then commenced labour, when the blood-pressure rose to 156/108 mm. Hg. Her daily urinary output immediately dropped from 92 ounces, containing a trace of albumin, to 20 ounces, containing 0.6 per cent of albumin (catheter specimen). During the next 17 hours she excreted four ounces of urine loaded with albumin. At this time thyroid extract gr. 4 was given, and a further gr. 2 eight hours later. During the next 24 hours she secreted 31 ounces of urine, which only contained a trace of albumin, although the blood-pressure remained at the same elevated level. Delivery occurred shortly after this. The blood-urea varied from 34 to 39 mgm. per cent.

What cannot be disputed is that the amount of albumin in the urine went up from a trace to 0.6 per cent, and that during the next 17 hours only four ounces of urine loaded with albumin were passed. Whether the thyroid had any effect on the secretion of urine in this case is immaterial, the fact that matters is that the amount of albumin in the urine went up from a trace to 0.6 per cent, and again fell to a trace before delivery. This fact could not be accounted for on the assumption that a pregnancy toxin had damaged the kidneys, but it is explicable on the view suggested above.

Hypertension.

Evidence is accumulating to suggest that the increased tone of the blood-vessels in hypertension is to be attributed either to a relative increase of pressor, or to a relative decrease of depressor substances circulating in the blood. It is generally admitted that a fall of blood-pressure normally occurs during the early months of pregnancy (Hare and Karn), and I have drawn attention to two facts, which, it is suggested, are of supreme importance. (1) That low blood-pressures, the systolic being below 90 mm. Hg., are commonly encountered during the first half of pregnancy in patients known to have a normal blood-pressure when not pregnant; (2) the blood-pressure falls during the first six months of pregnancy in patients known to suffer from hypertension.

Strong corroborative evidence of the fact that the blood-pressure falls during the early months of pregnancy is afforded by the fact that while a number of observers in this country and in the United States of America (Hare and Karn, Symonds,

Stocks) consider the normal blood-pressure of a healthy woman in the childbearing period to vary from 120/75 to 130/85 mm. Hg., Browne, in agreement with certain American obstetricians, states "that a rise of blood-pressure above the normal limit of 130/70 mm. Hg. is usually the earliest sign of pre-eclamptic toxaemia." It is of interest to note that Symonds's series 3.5 per cent of all the women who presented themselves for life assurance had a systolic blood-pressure exceeding 140 mm. Hg.

I have drawn attention to the group of patients whose blood-pressure rises, sometimes by 50 mm. Hg. as the result of applying the armlet, and have suggested that they possess jumpy adrenals. In this group of patients the diastolic blood-pressure also becomes elevated, and although the blood-pressure may return to the normal after rest, it is true to say that the jumpy adrenal may not infrequently progress to the true hypertensive type. One other well known fact may be mentioned, namely that patients with hypertension may show an elevation of blood-pressure after delivery which sometimes reaches a higher level than before delivery as late as seven days after the birth of the child. This elevation of the blood-pressure could not be attributed to any pregnancy toxin.

During 1935 30 patients were treated in the antenatal ward at St. Mary Abbot's Hospital for hypertension, and this figure excludes a considerable number of patients admitted for this condition, who responded rapidly to treatment and were discharged. Of these 30 patients 20 paid two or more satisfactory visits to the antenatal clinic, while 10 were admitted from outside sources, the toxaemic condition having been maintained for an unknown period of time. Of the 20 patients, 11 being primigravidae, who were kept in hospital until delivery occurred, only three passed small amounts of albumin in the urine when admitted. In one of these patients the albuminuria cleared up within three days, neither did it occur during her stay in hospital. Two further patients passed albumin in the urine during the 48 hours before delivery. Induction of labour was not carried out in any case, and with the exception of one case, to which reference will be made, no patient suffered from any symptom or oedema after the first few days in hospital. They all gave birth to living children, only one of which died during the neonatal period, and this infant had a malformed heart and showed transposition of the viscera. Three of these patients suffered from chronic glomerulo-nephritis, and seven patients went out of hospital with some elevation of the blood-pressure beyond the normal, but not,

with the exception of two of the patients suffering from nephritis, exceeding 145 mm. Hg.

On the other hand, it was not found possible to cause the blood-pressure to return to the normal before delivery except in three cases, whereas in some it rose considerably. It is my experience that, providing it is possible by dietetic treatment to clear up all the symptoms, hypertension unassociated with arterio-sclerosis is of no importance so long as the fluid intake of any one day is limited to the fluid output of the previous day. The extraordinary finding was that the most dramatic falls in the blood-pressure occurred in patients with chronic glomerulo-nephritis.

The main facts concerning the 10 cases, seven being primigravidae, admitted from outside sources will now be summarized. (*a*) All except one suffered from albuminuria. (*b*) Only two left the hospital with normal blood-pressures. (*c*) Three gave birth to premature, macerated infants. One infant died after extraction with the forceps, and labour was induced in one patient at the twenty-eighth week of pregnancy. (*d*) At least three of these patients suffered from definite chronic nephritis, while a fourth, a primipara, aged 26 years, had well-marked thickening of her brachial and radial arteries. (*e*) One of these patients developed a mild form of eclampsia. (*f*) Their time in hospital was relatively short. Those giving birth to stillborn infants were in the antenatal ward for 8, 11 and 14 days respectively.

Hereditary and Familial Factors.

I have recently drawn attention to the well-known fact that chronic nephritis and hypertension run in families (Theobald).[7] In investigating the cases of hypertension occurring during pregnancy I have been more than surprised at the frequency with which this condition is familial. This frequency may perhaps be best exemplified by giving a brief *résumé* of the relevant facts concerning the nine patients suffering from hypertension who are at one and the same time in either the antenatal or lying-in wards of St. Mary Abbot's Hospital as this paper is being written.

(1) R.K., 1-gravida, aged 28 years, six months pregnant, twin pregnancy, blood-pressure rising. Her father died from arterio-sclerosis and her mother has a high blood-pressure. Her sisters are not available for investigation.

(2) M.H., 2-gravida, aged 30 years, blood-pressure 160/100 mm. Hg. at delivery. Her mother, aged 59 years, has a blood-pressure of 170/90 mm. Hg. The rest of the family are not available for investigation.

(3) N.McE., aged 28 years, 1-gravida, twin pregnancy. Blood-pressure 170/120 mm. Hg. Mother has heart trouble, necessitating three months in bed last year. Family not available for investigation.

(4) E.G., aged 23 years, 1-gravida, pre-eclampsia from outside. History of scarlet fever, diphtheria, influenza, tonsillitis (tonsillectomy). Patient knows little about her family, the members of which are not available for investigation.

(5) G.Y., primipara, aged 25 years. Acid fast bacilli found in urine. Family not available for investigation.

(6) M.R., aged 34 years, 2-gravida, blood-pressure 200/120 mm. Hg., 32 weeks pregnant and in perfect health. Her unmarried sister, aged 26, has a blood-pressure of 155/80 mm. Hg., and a blood-urea of 44 mgm. per cent

(7) V.T., aged 23 years, 1-gravida, 36 weeks pregnant, blood-pressure 140/95 mm. Hg. Her mother died of a stroke and her father, aged 68, has a blood-pressure of 200/110 mm. Hg.

(8) M.M.B., aged 18 years, 1-gravida. Her father died from a stroke, and her mother suffers from high blood-pressure.

(9) V.O'G., aged 20 years, 1-gravida, blood-pressure 170/110 mm. Hg. Her mother died from a stroke at the age of 54, and her sister, aged 15, has a blood-pressure of 150 mm. Hg. and a blood-urea of 54 mgm. per cent.

It is thus evident that in six and possibly seven of the nine patients admitted because of a high or rising blood-pressure there is a familial history of hypertension.

The Investigation of Patients Suffering from Hypertension.

All patients attending the antenatal clinic whose blood-pressure rises to or exceeds 140 mm. Hg., or who pass albumin in the urine, or who are definitely not well, are admitted to the antenatal ward. The blood-pressure, fluid intake and output, and amount of albumin in the urine, if present, are chartered daily.

The Urine. The urine is cultured and examined for casts on several occasions, and Calvert's urea concentration test is invariably carried out.

Blood. A routine estimation of the blood-urea is made and invariably repeated. Estimations of the amounts of calcium, phosphorus, non-protein nitrogen, cholesterol and chlorides are frequently made. All the patients are kept on the diet reported elsewhere (Theobald).[6]

We have found that estimations of the blood-urea combined with a modification of Calvert's urea concentration test afford the most information in the study of these patients, although we believe that the water-diuresis test, accurately carried out, would be equally valuable. Except in patients with

chronic glomerulo-nephritis the blood-urea nearly always exceeds 40 mgm. per cent towards the end of pregnancy, while the figure for the urea concentration may be normal, although it is frequently low. I will instance the case of a girl, aged 23 years, at the moment in the gynaecological ward. Her systolic blood-pressure is 116 mm. Hg. and her urine is normal. Her blood-urea, however, is 42 mgm. per cent, and its maximal concentration, as shown by Calvert's test, is 2.85 per cent. Almost identical figures were obtained when these estimations were repeated. I am of the opinion that her blood-pressure will rise rapidly during the next few years, and that if she becomes pregnant she will suffer from hypertension. It is usually believed that the urea concentration test is a measure of renal competence but there is much evidence to suggest that this is not always or even normally the case. While it is true that if the kidneys are failing urea will concentrate in the blood, it is equally true that this substance will accumulate in the blood during anuria resulting from extra renal causes. Urea is formed in the liver, is a low threshold substance and subserves useful functions in the body, and it is reasonable to assume that its excretion, like that of water, is controlled by extra renal factors. It is not possible to develop this thesis here, but it is suggested that when in young people the level of the blood-urea lies between the figures of 40 and 100 mgm. per cent it may serve as an index of hepatic function, always providing glomerulo-nephritis can be excluded.

Cases Illustrating Special Points.

(1) *The patient who developed a mild form of eclampsia in hospital.*

B.M., aged 24 years, was admitted from outside with oedema, a blood-pressure of 140/90 mm. Hg. and 0.3 per cent of albumin in her urine. She had had scarlet fever, diphtheria and pleurisy. Investigation of her blood showed: cholesterol 160 mgm., creatinine 1.27 mgm., non-protein nitrogen 32.5 mgm., urea 51 mgm., and calcium 9.8 mgm. per cent. Eleven days later, when labour was just commencing, these estimations were repeated. There were no significant differences except that the urea had risen to 62 mgm. per cent and the calcium had dropped to 9 mgm. per cent. Examination of the cerebrospinal fluid showed chlorides 740 mgm. per cent, urea 42 mgm. per cent, and calcium 4.40 mgm. per cent. The blood-pressure had risen to 170/100 mm. Hg., but had been higher two days previously. Two fits occurred the next morning immediately before delivery. Twelve hours later two further fits followed the passage of a catheter. The blood-pressure returned to the normal, the albuminuria cleared up, but even six months later the blood-urea was just under 40 mgm. per cent, although she was able to concentrate this

substance well. The infant, a male weighing 8 pounds 12 ounces, gained weight before leaving the hospital. Owing to an oversight, her fluid intake was not regulated, and it is reasonable to assume that her fits were due to water intoxication.

Two cases illustrating the necessity for a complete investigation of the patient.

L.H., aged 32 years, 3-para, 26 weeks pregnant, was admitted on the 9th September 1935, with a blood-pressure of 150/100 mm. Hg., but complaining of no symptoms. Her blood-pressure fell to 116/80 mm. Hg., and she appeared to be in good condition. Intravenous pyelography showed a very poor secretion of unroselectan, and her blood-urea rose from 69 to 79 mgm. per cent in the course of a few days, the non-protein nitrogen being 53 mgm. per cent. Her maximal concentration of urea was 1.05 per cent (the normal being 4.5 per cent). The uterus was, therefore, emptied. She did not give any history of scarlet fever, and casts were never found in her urine. The point of interest about her was that the blood-pressure came steadily down to the low figure of 116/80 mm. Hg., when on the special diet, and then rose after the uterus was emptied and remained at the level of 146/90 mm. Hg. until her discharge. It may also be noted that were it not for (a) intravenous pyelography; (b) the estimations of her blood-urea; and (c) the urea concentration test, there would have been no indication for terminating the pregnancy, a necessary procedure in her case.

E.B., aged 26 years, 1-gravida, admitted on the 20th May, 1935, two months after her symptoms had first commenced. Her blood-pressure was 202/120 mm. Hg., her urine contained albumin 0.5 per cent, and she showed very marked oedema reaching to the knees. She complained of severe headaches which disappeared within two or three days. She was very anaemic (r.b.c. 2½ million, haemoglobin 40 per cent). Delivery occurred on the 4th June, after a long labour terminated with the forceps, which resulted in the death of the child. Estimations of the blood-urea showed: 27th May, 57 mgm. per cent; 3rd June, 76 mgm. per cent; 24th June, 91 mgm. per cent; 1st October, 57 mgm. per cent. Examination of the cerebrospinal fluid on the 1st June showed: urea 35 mgm. per cent, chlorides 720 mgm. per cent, and calcium 6.35 mgm. per cent. The albumin disappeared from the urine, but her blood-pressure remained elevated (150/110 mm. Hg. per cent) as did her blood-urea. Hypertension in this case was associated with a high blood-urea, but there was not any history of scarlet fever, diphtheria or tonsillitis, neither could a familial history of hypertension be elicited.

Cases of glomerulo-nephritis.

W.N., aged 28 years, was admitted 25th January, 1935, with a blood-pressure of 146/90 mm. Hg., albuminuria and complaining of severe headaches. Her previous history showed that she had suffered from scarlet fever, diphtheria, rheumatic fever, and had had several attacks of kidney trouble. The albuminuria and headache persisted after her delivery,

and the blood-pressure remained remarkably constant for several weeks after delivery at 150/110 mm. Hg. This was a clear case of glomerulo-nephritis, and it is worthy of note that the albuminuria disappeared during the early months of pregnancy. Her blood-urea was only 33 mg. per cent.

L.D., aged 44 years, 5-gravida, giving a history of scarlet fever, was admitted on the 17th February, 1935, with a blood-pressure of 200/100 mm. Hg., very marked oedema to the knees, and 1.3 per cent of albumin in the urine. All her symptoms cleared up before delivery, which occurred 11 days later; the foetus was macerated. She was discharged with a blood-pressure of 140/100 mm. Hg (not very high for a woman of her age), and a mere trace of albumin in the urine (0.02 per cent). Her blood-urea did not exceed 27 mgm. per cent, but a large number of granular and hyaline casts were found in the urine on every occasion that it was examined. In other cases casts were found in the urine, although the blood-pressure was normal and albumin was not present in the urine.

The one case whose symptoms failed to clear up in the antenatal ward.

B.S., aged 27 years, primigravida, was admitted on the 12th September, when 35 weeks pregnant, for severe hyperemesis. She had had oedema of her legs for one month, and headaches, and albumin was present in her urine. Her blood-pressure was 128/100 mm. Hg. The symptoms, together with the albuminuria, cleared up in 48 hours. At the beginning of October the headaches became troublesome again, and she vomited frequently, so that she was not able to take either the diet or the extra substances. A few days later the blood-pressure began to rise and the symptoms became worse. The following report was received regarding the X-ray examination of the stomach made before her discharge: "The first part of the duodenum is spastic and irritable. It did not fill out at any time. Appearances indicate an ulcer of the first part." During the last 2½ years it has been found possible to cure hyperemesis in all but six patients, and in five of these evidence of some gastric lesion has been obtained subsequent to normal delivery. It is believed that the symptoms of this patient are to be attributed to her inability to take the necessary diet because of her duodenal ulcer.

Discussion.

The conception that pregnancy throws a great strain on the kidneys is irrational, for the oxygen consumption of the foetus *in utero* is very small (Barcroft). The strain of pregnancy is anabolic rather than katabolic, and on the liver rather than on the kidneys, and is comparable to that imposed by rapid growth of the child at puberty. If proof were needed for this obvious assumption it is provided by the fact that a normally functioning kidney may be removed at the fifth month of pregnancy without

causing any measurable strain on the remaining kidney (Theobald).[7] The first physiological function to be grossly disturbed in the second halt of a normal pregnancy is that of water elimination. It has been recently shown (Theobald and Verney) that the alteration in the night and day urine ratio which often proceeds until it exceeds unity may in large measure be accounted for on mechanical grounds. It is, however, easy to see that this disturbance of the water balance of the body normal to the latter half of pregnancy might proceed until, as frequently happens, the tissues retain more than the usual amount of water, a condition capable of resulting in oedema. This frequent passage of an excess of water into the tissues, even though it is excreted by night, tends to alter the permeability of the capillaries and thus initiates a vicious circle, which may end in oedema and convulsions.

It has also been shown (Theobald)[6] that many, if not most, pregnant women are unable during the latter half of pregnancy, even when lying in bed, to excrete a given amount of water with the same rapidity or to attain the same peak of urinary secretion as in the normal state.

This alteration in the water diuresis curves associated with the latter half of pregnancy might conceivably be due to an increase of antidiuretic substance or to a decrease of diuretic substance circulating in the blood-stream. Anselmino and Hoffmann offered experimental evidence to show that an increase of post-pituitary antidiuretic substance was present in the blood in the pre-eclamptic states. Theobald[5] confirmed the fact that an antidiuretic substance could be recovered from the blood of such patients, but showed that it could not be post-pituitary extract. It is, however, certain that the factor, or factors, which lead to water retention in the tissues, oedema and the convulsions of water intoxication are extra-renal and not renal. The kidneys have not any responsibility in the matter.

Numerous obstetricians have recognized for many years that hypertension is usually associated with albuminuria and is the more important condition, but to Browne belongs the credit for insisting that the hypertension almost invariably precedes the albuminuria. Although I am not prepared to accept his standard of normality or to subscribe to the view that there are no exceptions to the rule, there can be no doubt that in the great majority of cases a rise both in the systolic and the diastolic blood-pressures precedes the proteinuria. It is suggested that in London at least pregnancy hypertension has more often than not

a familial association. This fact, taken in association with the fact that the mortality rates for chronic nephritis are approximately the same for single and married women, makes it reasonable to assume that the causative factors which operate during pregnancy are those which operate in single women and in men. It may, therefore, be conjectured that the hypertension of pregnancy is an exaggerated picture of a process which proceeds slowly and relentlessly until it ultimately causes death from renal or circulatory failure or from cerebral haemorrhage.

It has been shown that the hypertension of pregnancy is normally preceded by a disturbance of the water balance of the body (which may in itself cause an elevation of the blood-pressure) and followed by proteinuria. It is my belief that this sequence of events may be attributed to the presence of abnormal or hetero-proteins in the blood. We do not know where the proteins normally circulating in the blood are formed nor how their amounts in the blood-stream are controlled, but it is reasonable to assume that both of these functions may be ascribed to the liver. This view does not violate any physiological principle nor is it contradicted by any clinical fact.

The hypothesis I have advanced to explain the toxaemias of pregnancy is based on their geographical distribution. Wherever the incidence of the toxaemias of pregnancy is high, there may be found a high incidence of hypertension, appendicitis, gall bladder disease, gastric and duodenal ulcer and carcinoma affecting the gastro-intestinal tract. (Compare relevant figures for Egypt and England.) It is generally agreed that a high incidence of the toxaemias of pregnancy is associated with a high intake of meat, and there is hardly an antenatal clinic where meat is not prohibited to a patient manifesting hypertension. The steep fall in the incidence of the toxaemias of pregnancy in Germany during the last two years of the Great War, when proteins were difficult to obtain, is convincing evidence in favour of this contention. It has, moreover, been reported that serious hepatic lesion may be caused in dogs by feeding them on a lean meat diet (Theobald).[1] On the other hand, I have shown that a very high animal protein diet may be given to these patients with nothing but benefit, providing a high intake of the vitamins and minerals be assured, and in particular of calcium, and vitamins B and D. It is, therefore, my belief that hypertension leading to pre-eclampsia is in the majority of cases to be attributed to an excessive intake of meat associated with a deficient intake of the vitamin B complex and a deficient assimilation of calcium. This

sequence of events is more liable to occur in women who have an inborn error of metabolism—an hepatic weakness which is usually familial.

It follows that there are two main groups of women who will develop pre-eclampsia and eclampsia: (i) those with chronic glomerulo-nephritis resulting from the exenthamata and tonsillitis; (ii) those with no renal damage. Practically all the women in this latter group have (apart from pregnancy) a blood-urea of or exceeding 40 mgm. per cent, and many show an inability to concentrate this substance adequately in the urine. Many, if not the majority of these women, moreover, have a family history of hypertension, but it is clear that relatively normal women will develop pre-eclampsia for the same reasons if the diet is grossly inadequate. It follows that the more adequate the antenatal care the higher will be the percentage of "toxaemic" patients who will manifest recurrence of symptoms in succeeding pregnancies.

It may, therefore, be concluded that the more thoroughly women suffering from the albuminuria of pregnancy are investigated the less possible it will be to maintain the thesis that there is any causal relation between pregnancy and chronic nephritis. Seeing that the nephritis of pregnancy was attributed to a pregnancy toxin the abandonment of this view will make the existence of such a toxin not only less plausible but unnecessary.

I wish, in conclusion, to thank Professor James Young, under whose care these patients were, not only for permission to undertake their treatment but for his interest in the investigation. My sincere thanks are also due to the Medical Superintendent, Mr. J. Carver, for all the facilities he has granted and for his realization of the necessity for an adequate number of antenatal beds. It is, moreover, my privilege to thank Sir Frederick Menzies, Chief Medical Officer of the London County Council, for permission to publish data concerning patients at St. Mary Abbot's Hospital.

Summary.

1. Women who normally suffer from albuminuria tend to pass a protein-free urine during the first six months of pregnancy.

2. The blood-pressure normally falls during the first half of pregnancy, and the blood-pressure of women suffering from hypertension may fall within normal limits during this period of gestation.

3. The water balance is disturbed during the second half of a

normal pregnancy. This disturbance precedes hypertension which itself precedes albuminuria.

4. This sequence of events may be caused by hepatic malfunction and be the result of abnormal proteins circulating in the blood.

5. The albuminuria is usually the result of these extra-renal factors, the kidneys themselves being functionally and structurally normal.

6. The hypertension of pregnancy usually associated with a blood-urea exceeding 40 mgm. per cent, and frequently with the failure of the kidneys to concentrate this substance adequately. (This applies when the patients receive an ordinary diet.)

7. It is suggested that this high blood-urea may be considered an index of hepatic malfunction.

8. There are two main groups of women in whom it is possible to predicate before marriage that they are likely to suffer from pre-eclampsia or eclampsia, (*a*) those with glomerulo-nephritis resulting from the exenthamata and tonsillitis; (*b*) those with a blood-urea exceeding 40 mgm. per cent. and who are unable to concentrate this substance in the urine. These women will, apart from suitable treatment, manifest toxaemic symptoms in each successive pregnancy.

9. It is suggested that the hepatic malfunction resulting in the presence of abnormal proteins in the blood-plasma is caused by a meat diet associated with a disturbance of the calcium metabolism and an insufficient intake of the vitamin B complex.

10. Whereas this sequence of events may occur in any woman as the result of the above errors in diet, it is more likely to occur in women with an inborn error of metabolism which is hereditary.

11. The remarkable association of heredity with the hypertension of pregnancy makes it reasonable not only to place this condition in the same category as hypertension occurring in the non-pregnant state, but warrants the assumption that the hypertension of pregnancy is merely an exacerbation of the insidious process which ultimately results in death.

12. There is no evidence of any causal relation between pregnancy and chronic nephritis.

13. A woman with chronic glomerulo-nephritis may pass through pregnancy without further damaging her kidneys providing that the condition has not progressed sufficiently far to embarrass her general health and that certain tests for renal efficiency prove satisfactory.

sequence of events is more liable to occur in women who have an inborn error of metabolism—an hepatic weakness which is usually familial.

It follows that there are two main groups of women who will develop pre-eclampsia and eclampsia: (i) those with chronic glomerulo-nephritis resulting from the exenthamata and tonsillitis; (ii) those with no renal damage. Practically all the women in this latter group have (apart from pregnancy) a blood-urea of or exceeding 40 mgm. per cent, and many show an inability to concentrate this substance adequately in the urine. Many, if not the majority of these women, moreover, have a family history of hypertension, but it is clear that relatively normal women will develop pre-eclampsia for the same reasons if the diet is grossly inadequate. It follows that the more adequate the antenatal care the higher will be the percentage of "toxaemic" patients who will manifest recurrence of symptoms in succeeding pregnancies.

It may, therefore, be concluded that the more thoroughly women suffering from the albuminuria of pregnancy are investigated the less possible it will be to maintain the thesis that there is any causal relation between pregnancy and chronic nephritis. Seeing that the nephritis of pregnancy was attributed to a pregnancy toxin the abandonment of this view will make the existence of such a toxin not only less plausible but unnecessary.

I wish, in conclusion, to thank Professor James Young, under whose care these patients were, not only for permission to undertake their treatment but for his interest in the investigation. My sincere thanks are also due to the Medical Superintendent, Mr. J. Carver, for all the facilities he has granted and for his realization of the necessity for an adequate number of antenatal beds. It is, moreover, my privilege to thank Sir Frederick Menzies, Chief Medical Officer of the London County Council, for permission to publish data concerning patients at St. Mary Abbot's Hospital.

Summary.

1. Women who normally suffer from albuminuria tend to pass a protein-free urine during the first six months of pregnancy.

2. The blood-pressure normally falls during the first half of pregnancy, and the blood-pressure of women suffering from hypertension may fall within normal limits during this period of gestation.

3. The water balance is disturbed during the second half of a

normal pregnancy. This disturbance precedes hypertension which itself precedes albuminuria.

4. This sequence of events may be caused by hepatic malfunction and be the result of abnormal proteins circulating in the blood.

5. The albuminuria is usually the result of these extra-renal factors, the kidneys themselves being functionally and structurally normal.

6. The hypertension of pregnancy usually associated with a blood-urea exceeding 40 mgm. per cent, and frequently with the failure of the kidneys to concentrate this substance adequately. (This applies when the patients receive an ordinary diet.)

7. It is suggested that this high blood-urea may be considered an index of hepatic malfunction.

8. There are two main groups of women in whom it is possible to predicate before marriage that they are likely to suffer from pre-eclampsia or eclampsia, (*a*) those with glomerulo-nephritis resulting from the exenthamata and tonsillitis; (*b*) those with a blood-urea exceeding 40 mgm. per cent. and who are unable to concentrate this substance in the urine. These women will, apart from suitable treatment, manifest toxaemic symptoms in each successive pregnancy.

9. It is suggested that the hepatic malfunction resulting in the presence of abnormal proteins in the blood-plasma is caused by a meat diet associated with a disturbance of the calcium metabolism and an insufficient intake of the vitamin B complex.

10. Whereas this sequence of events may occur in any woman as the result of the above errors in diet, it is more likely to occur in women with an inborn error of metabolism which is hereditary.

11. The remarkable association of heredity with the hypertension of pregnancy makes it reasonable not only to place this condition in the same category as hypertension occurring in the non-pregnant state, but warrants the assumption that the hypertension of pregnancy is merely an exacerbation of the insidious process which ultimately results in death.

12. There is no evidence of any causal relation between pregnancy and chronic nephritis.

13. A woman with chronic glomerulo-nephritis may pass through pregnancy without further damaging her kidneys providing that the condition has not progressed sufficiently far to embarrass her general health and that certain tests for renal efficiency prove satisfactory.

14. A woman may consistently pass granular and hyaline casts in her urine, even while at rest in bed, although it contains no protein and her blood-pressure is normal.

15. Death of the foetus *in utero* is to be attributed to dietetic deficiencies.

16. If it be true that the hypertension of pregnancy presents an exaggerated picture of the march of hypertension in man, then it is obvious that the obstetrician has the unique opportunity of contributing to our knowledge of the early stages of chronic glomerulo-nephritis and of the causation of some forms of arterio-sclerosis and renal failure, for he sees the patient 10 years before she consults the physician with symptoms attributable to the condition.

17. If there is not any causal relation between pregnancy and chronic nephritis the last need for postulating a pregnancy toxin has disappeared.

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Achlorhydria as an aetiological factor in Pruritus Vulvae, associated with Kraurosis or Leucoplakia.*

BY

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PRURITUS VULVAE is a very common symptom and one which sometimes is very difficult to cure. It is in these intractable cases that changes in the skin of the vulva take place. These changes have been called by many names such as leucoplakia, kraurosis vulvae, and leucoplakic vulvitis. I hope to be able to show that a common factor is present in these conditions, and that this factor is an achlorhydria which causes a deficiency of absorption of vitamin A from the diet.

Changes in epithelial structures result from this deficiency. These skin changes do not always conform to the same clinical type but depend on the stage of the disease, and so in the past they have been given many different names. However, the original cause is the same in all types. Occasionally an achlorhydria is not present, and it has been found that in these cases the diet itself is deficient in vitamin A.

Literature.

Kraurosis and leucoplakic vulvitis have been classed by Taussig[1] under the heading of atrophic diseases of the vulva. A few years ago it was thought that these two conditions were quite distinct, and the conditions of kraurosis was considered to be a lesion of the vulva which started in women after an artificial or natural menopause. It was distinguishable by a shrinking of the parts around the vulval orifice. The labia majora, perineum and peri-anal regions were not involved.

In leucoplakic vulvitis, however, the vulva was involved in part or in whole, and the characteristic sign was the formation of thickened whitish areas of epidermis.

* Part of a thesis for the Degree of M.D. of the University of Cambridge, May 1936.

I have been unable to confirm the observations of Berkeley and Bonney,[2] who described four stages of the disease, and who in 1899 emphasized the fact that leucoplakia was a pre-cancerous condition and advised excision of the vulva. The conditions of the vulva which I have found can be grouped under headings of hypertrophy and atrophy.

The histopathology of the condition and its variations have been frequently described in the literature, more especially by Taussig. However, nowhere have I been able to find any mention of the aetiology of the condition, and as Taussig[3] says: "We are still far from a satisfactory answer as to the why and the wherefore." He called the condition a chronic atrophic inflammatory one.

Sabre-Casas and Carranza[4] stated that the aetiology had not yet been discovered, but they seemed quite certain that there was a definite sequence, namely pruritus, leucoplakia, kraurosis, and, lastly, epithelioma. These authors described in detail the pathological changes, and proved to their satisfaction that all the lesions were pre-cancerous, and for that reason they advised excision of the vulva in all cases.

Most of the other literature on the subject has dealt only with the clinical and pathological findings and the various treatments, without mentioning anything new in the way of the causation of the conditions. Montgomery, Counsellor and Craig[5] described in detail the histopathologic picture of kraurosis, leucoplakia and pruritus vulvae, and said that it was possible to distinguish the conditions both clinically and microscopically, and that one condition might occur independently of the other two. However, they said that two or all three might be present together, or might merge into one another, especially as all three were likely to appear in the later decades of life. They also considered that leucoplakia and kraurosis were pre-cancerous.

Davidson[6] stated that careful study, of his own and other cases reported, revealed not one factor which could be designated as an aetiological agent. Wilson[7] did not mention the aetiology of the condition in his paper, but referred to the treatment by injections of alcohol. Other papers by Regnard,[8] Gasquet,[9] Cattrell,[10] and Glass[11] all referred to treatment and did not mention the cause.

I wish to quote rather fully from a paper which has just lately been published in *Surgery, Gynecology and Obstetrics* of October 1935, by Adair and Davis.[12] These authors had described in detail the conditions on which I was writing this part of my thesis. However, it was interesting to find that fresh light

had not been thrown by them on the aetiology of the conditions nor on their treatments. The description of their cases tallied exactly with those which I had observed, and they published some excellent coloured pictures which could have been copied from my own cases.

They stated that the terms kraurosis and leucoplakic vulvitis had all been used by various authors describing progressive pathological atrophic changes in the vulva, and that these terms only represented various stages of the disease which ultimately ended in epithelioma. I entirely agree with these conclusions.

The authors have described three stages, but I have been unable to follow my cases so as to try and find out the sequence of the changes which they have noted. My cases have all been treated medically as soon as diagnosed. The third stage of Adair and Davis, in which the labia minora had disappeared completely, and which they stated was the final stage of advanced atrophy, was noticed in one of my patients who was a woman (Fig. 8) of only 27 years of age and who had had pruritus for only three years. She may, of course, have already passed through the hypertrophic stage of Adair and Davis before coming under my notice.

The incidence in their series was 0.24 per cent in 9,682 gynaecological patients, but they stated that perhaps several early cases of pruritus might have been missed. I have been able to collect 42 cases during the last few years, but I must add that I am now able to diagnose the condition at a very much earlier stage, and so the majority of cases have been seen during the last two years.

These authors have excised the vulva in nine cases and so have been able to obtain specimens for microscopic work. I, unfortunately, have been unable to obtain specimens, as my treatment has been medical. However, there is a large amount of literature on the histological side of these conditions, and the changes have been described in detail.

They quoted that infection of the vulva caused the pruritus, but I think that the infection is secondary to the presence of the common factor which allows the skin to become easily infected, and this factor is the lack of absorption of vitamin A, which results in an abnormal type of vulval skin which is easily infected and irritated. This alteration in the skin is not only noticed in the vulva but can easily be found in other situations, such as the skin of the forearms, hands and neck. Dr. Eugene McLaughlin, with whom I have been working on this subject, is shortly

publishing a paper on the alterations in the skin in vitamin A deficiency. The authors have not made any mention in their paper of these associated cutaneous lesions.

Under prognosis they stated that the disease progresses with the possible development of carcinoma. This result has, I think, been definitely proved to be so by Berkeley and Bonney and Sabre-Casas and Carranza.[4]

No new treatment had been advocated by Adair and Davis, as the real cause had not been found. Excision of the vulva had given excellent relief of symptoms, but other forms of treatment, such as the application of ointments and X-ray treatment, only gave temporary relief. I would like to mention a warning against radiation therapy. The action of X-rays on an already undernourished skin often results in a very acute exacerbation of the inflammation, which takes a long time to settle down, and afterwards the irritation is often not relieved.

I have quoted Adair and Davis very fully for two reasons, firstly because their paper is the latest that I have been able to find, and, secondly, the syndrome described by them is identical with the one that I have had under observation since I quoted my cases in 1932.[13] I feel that the points of aetiology and treatment, which I shall raise, will be able to be more appreciated after this digest of their paper.

History of Investigation.

My attention was first drawn to this subject during the year 1931. I was consulted by a patient aged 43 years, who complained of vulval irritation which she had had for 12 years. The irritation had first been noticed while she was pregnant, and it had persisted ever since despite numerous treatments. On examination there were white patches of leucoplakia over both labia minora and an area of white thickened shiny skin running across the perineum. I diagnosed the condition as one of leucoplakia and advised excision of the vulva. However, before deciding to perform the operation I admitted the patient to hospital for further examination, as she had often had a sore tongue, and there was a very strong family history of pernicious anaemia. A test meal was done, and the report stated that there was not any free hydrochloric acid present. The report on her blood was a colour index of 1.1, haemoglobin 85 (N=90), red cells 3,860,000. The film showed anisocytosis with a tendency towards megalocytosis.

The patient was given large doses of iron and liver and dilute

hydrochloric acid was ordered to be drunk at meals. The operation was postponed and her irritation gradually improved. Much to my surprise I found that the condition of the labia had altered and the patches of leucoplakia had disappeared. I saw her a few weeks ago (on December 12th, 1935) and she had not had any irritation for 15 months. The condition of her vulva had quite changed, and at that time there was absolutely no whitening nor thickening, in fact, the vulva appeared to be that of a normal woman of 30. Unfortunately, this case was a private one, and I was unable to obtain photographs of the vulva.

During 1931 I saw several similar cases, and in 1932 I published a short paper on the subject in the *Medical Journal of Australia*.[13] At that time I had thought that the lack of free hydrochloric acid in the stomach was the cause of the pruritus. All the cases which had been noted at that time had had numerous treatments, and the pruritus had usually first been noticed during a pregnancy. I came to the conclusion that these patients had had an anaemia of pregnancy with the usual low secretion of acid and that their general health had not improved after the birth, with the result that the vulval skin had become altered and so easily irritated.

From this beginning I have found the conditions of achlorhydria in a large number of patients suffering from pruritus vulvae. It has not been possible to persuade every patient to have a test meal, but in the 42 cases which I have placed under this heading 35 have had test meals.

I had thought at the beginning that I was at last on the track of a cure for these unfortunate people who had so often been called neurotic. However, some patients improved on taking dilute hydrochloric acid while others did not improve.

During the course of routine gynaecological practice I had noticed in the large majority of cases suffering from pruritus and discharge that as soon as the discharge became less the irritation also got less. However, in a few cases the cure of the discharge did not relieve the irritation. In this type of case a test meal was done and achlorhydria was nearly always found. In these cases there was, therefore, a primary cause for the changes in the skins which made them more susceptible to the discharge, and, therefore, the discharge was not really the primary cause of the pruritus but only an activating one.

In 1934 Dr. Eugene McLaughlin, the Director of the Laboratory at the Adelaide Hospital, had interested himself in the subject and had been doing the test meals for me. He had been

searching the literature for the effect of deficiency of various vitamins on the skin and epithelial tissues, and had found two papers on the subject, one by Klusmann and Simola,[14] and an earlier article by Wolbach and Howe,[15] who had stated that female guinea-pigs, which had been fed on a diet deficient in vitamin A, had vaginae which usually contained accumulations of keratinized cells and frequently the epithelium was thickened and shaggy. Both these papers suggested that a lack of vitamin A caused hyperkeratosis. Dr. McLaughlin suggested that a vitamin A preparation be given to some of my patients.

I decided to try its effect on a patient I had been endeavouring to cure for months. The patient, a woman aged 25 years, had reported complaining of very bad pruritus of several years standing with a vaginal discharge and a skin disease in her pubic hair and down between her thighs. The discharge was cured by cauterizing an erosion of her cervix, and it was found that the skin lesion was caused by a tinea. The discharge and tinea had been cured, but still she had bad irritation. There were two spots of leucoplakia on the anterior ends of the labia minora just before they reached the prepuce of the clitoris. Her mother, aged 64 years, had also complained of severe pruritus for 20 years, but she had never been examined. She was found to have a very marked hypertrophic keratosis of the whole of her vulva. The vulva was excised and the irritation disappeared. The daughter did not want to have this done as she was engaged to be married. However, she was persuaded to have a test meal, and she was found to be suffering from achlorhydria. Her mother also had no free acid in her stomach. She was put on acid but without relief. On Dr. McLaughlin's suggestion she was given a teaspoonful of cod-liver oil three times a day, and the acid was stopped. She reported a week later and said that the oil made her sick and that she could not digest it. She was given acid as well as the oil. She reported a fortnight later saying that her irritation was ever so much better and that she could digest the oil. Having married she is still taking oil and acid, and is now pregnant, and the irritation has returned slightly.

It was deduced that she was a woman who could not absorb vitamin A owing to the lack of acid in her stomach. The lack of vitamin A started changes in the vulval epithelium, and the vaginal discharge was the cause of the mild infection of the skin and so of the irritation. This result was most encouraging, and I started ordering test meals in cases of intractable pruritus.

The diet of the average South Australian woman contains a

quantity of vitamin A, so that it cannot be the lack of vitamin A in the diet, but I think the vitamin A is not absorbed from the food owing to the lack of acid in the stomach. To make sure that the woman is getting enough vitamin A, cod-liver oil is given as well. In my private cases I am giving capsules of hallivol made by Parke Davis.

The next step in the investigation was to look for other signs of vitamin A deficiency in these cases of pruritus, such as the presence of spoon-shaped and brittle nails, powdery skins, and hyperkeratosis in other parts of the body. These signs have been noted in nearly every case.

Finally, I am investigating cases of epithelioma of the vulva on the above lines. Most cases of epithelioma complain of long-standing pruritus, and I am ordering test meals on all cases admitted to the wards, but as these cases are rare, I have not collected sufficient data to say anything about them.

Vulval Changes.

The local changes of the vulva in these cases of achlorhydria with vitamin A deficiency are very variable and are not produced in any definite sequence. I have divided them into two main groups: (*a*) hypertrophic conditions, (*b*) atrophic conditions. I have been unable to determine which condition arises first, or whether one condition, if allowed to progress long enough, will change into the other, or vice versa.

Adair and Davis[12] described three stages, and stated that the last stage was one of atrophy, but I have been unable to confirm or disprove their conclusions.

(*a*) *Hypertrophic Conditions.*

This group I have divided again into two types.

Type 1. In the first type the skin of the labia majora has become thickened, corrugated, roughened, and in some cases it has become whitened. The consistence has changed and the subcutaneous tissues have become firmer. This thickening also extends on to the outer surfaces of the labia minora, and they have become hypertrophied and thickened. This type of the hypertrophic condition is the commonest one in my series, and is well illustrated in Fig. 1.

Type 2. In the second type the skin on the inner surfaces of the labia minora has been involved as well. These surfaces are covered with raised whitish areas of so-called asbestos-looking material. This is really heaped up epidermis and has been called leucoplakia. These areas of leucoplakia can exist all over the

inner surfaces of the labia or only in one or two places. Again, the actual tissue of the labia minora can be involved as localized spots of firm white tissue. This type was not so common in my series and is illustrated in Figs. 2 and 3.

These two types, however, often occurred in the same patient, but the preponderance of one type often overshadowed the other type.

Infection of hypertrophic conditions. Infection can be superimposed on either type. In the first type the skin over the labia minora and outer sides of the labia minora becomes much inflamed and reddened. The skin becomes a raw weeping area which exudes a sero-purulent discharge. The treatment of the infection is difficult, as the skin, on which the infection has gained a hold, is one which is poorly nourished. The treatment of the original condition must be instituted at once as well as the treatment of the local infection. This infective condition is illustrated in Fig. 4.

In the second type infection usually causes ulceration of the inner surfaces of the labia, due, I think, to trauma of scratching, and this ulceration is well shown in Fig. 3.

Details of Case illustrated in Fig. 1.

This case demonstrates type 1 of the hypertrophic condition.

Mrs. E. P., aged 64 years, had complained of vulval irritation for 29 years. She had had innumerable treatments without relief. Her menopause had occurred about 20 years ago. She was otherwise a healthy woman. On examination the vulval condition was typical. The skin of the labia majora was thickened, whitened, and corrugated. (Fig. 1.) Her nails were spoon-shaped and brittle. The skin on the back of her hands and forearms was much thickened and of the texture of buckskin. (Figs. 7 and 8.) Her lips were a bluish colour and were often cracked. She was sent at once for a test meal, and the report showed that free acid was not present. She was given dilute hydrochloric acid and cod-liver oil. She is now completely free from irritation and states that the general condition of her skin is ever so much better. It is much softer and has lost its rough feeling.

Details of Case illustrated in Figs. 2 and 3, demonstrating Type 2.

Hypertrophic condition of the vulva with leucoplakic changes.

Mrs. McC., aged 32 years, had complained of vulval irritation for 10 years; she was otherwise a healthy young woman. On examination the vulva showed hypertrophy of the skin over the labia majora, but also marked heaped-up whitened areas over the inner surfaces of the labia minora. There were several areas of ulceration and the labia minora themselves were thickened. She had a glazed tongue, but other associated skin lesions were not present. A test meal was given, and the report was that "no free acid was present". She was given oil and acid and improved; the leucoplakic

FIG. 1.

TYPICAL HYPERTROPHIC CONDITION OF VULVA. TYPE 1.

Showing thickening and whitening of skin over labia majora. The skin is corrugated and firm.

FIG. 2.

HYPERTROPHIC CONDITION OF VULVA. TYPE 2.

Showing whitening and thickening of skin of labia majora. Leucoplakic spots seen with ulceration between inner upper ends of labia minora.

FIG. 3.

HYPERTROPHIC CONDITION OF VULVA. TYPE 2.

Labia minora separated, showing leucoplakia with ulceration of inner surfaces of labia minora.

FIG. 4.

INFECTION OF HYPERTROPHIC CONDITION OF VULVA. TYPE 1.

Skin over labia majora red, inflamed, weeping with sero-purulent exudate. Labia minora swollen and inflamed. (Whitish areas are due to reflected light on the weeping inflamed skin.)

FIG. 5.

ATROPHIC CONDITION OF VULVA IN WOMAN AGED 27.

The disappearance of labia minora with whitening and thinning of vulval and perineal skin can clearly be seen. Urethral orifice is enlarged and inflamed owing to trichomonas infection.

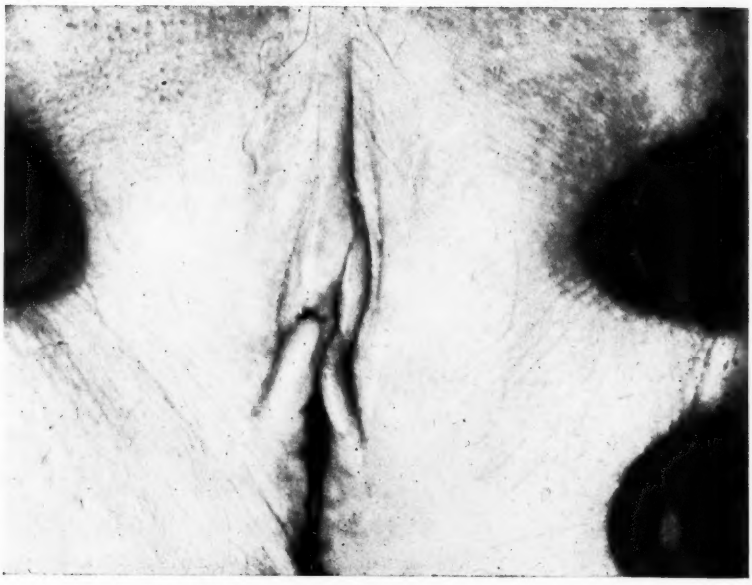

FIG. 6.

ATROPHIC CONDITION OF VULVA IN WOMAN AGED 70.

The labia minora are smooth, small, and white.

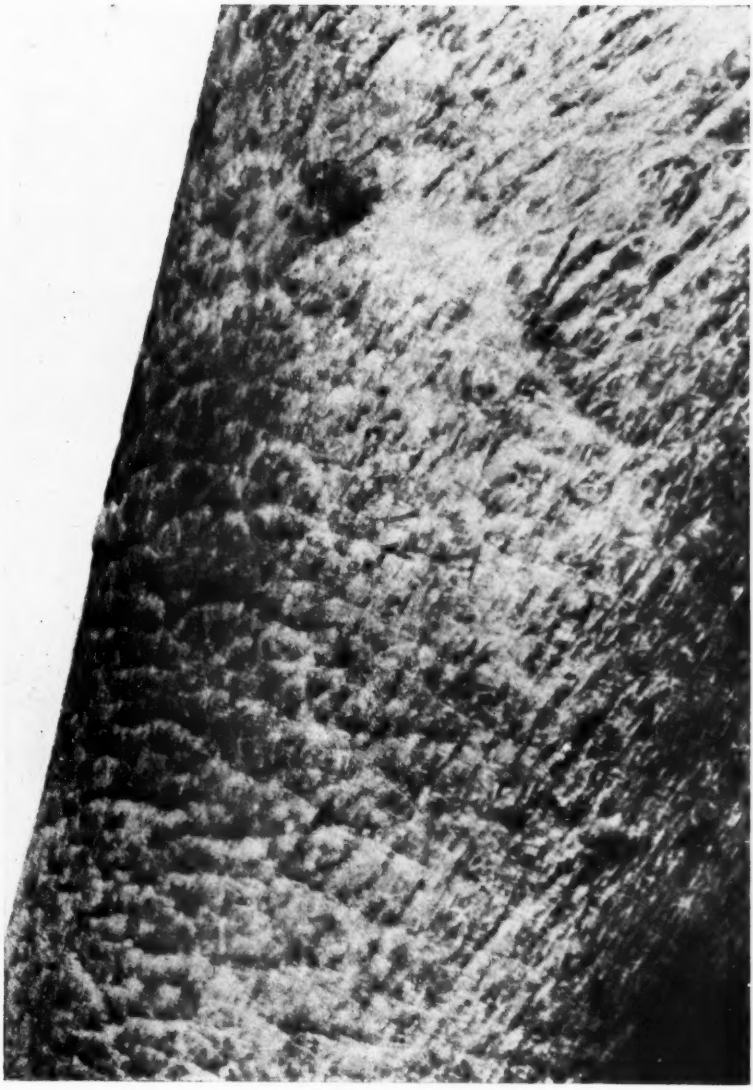

FIG. 7.

SKIN OF FOREARM OF CASE ILLUSTRATED IN FIG. 1.

Skin of forearm in hypertrophic condition of vulva, showing typical thickened skin, usually brown in colour, with very poor elasticity.

FIG. 8.

HANDS OF CASE ILLUSTRATED IN FIG. 1.

Skin on back of hands in hypertrophic condition of vulva, showing marked thickening with loss of elasticity.

condition disappeared. However, she reported again to say that she was as bad as ever. It was then ascertained that she had not been taking the acid regularly. The necessity of keeping strictly to her treatment was impressed on her, and the condition has improved again.

(*b*) *Atrophic Conditions.*

Atrophy of the vulva normally occurs in women after the menopause without causing pruritus, and an advanced stage of this condition is often seen, more especially, however, after an artificial menopause. This condition is usually called kraurosis. However, when pruritus is present with atrophy of the vulval skin, a pathological condition has arisen, and it is in this type that achlorhydria is very often found.

The skin of the labia majora becomes white and shiny, and appears to be very thin. The subcutaneous tissues also become atrophied and firmer. The skin over the perineum and fourchette usually becomes involved in the process and becomes white and thin. Cracks and abrasions occur and the pruritus is usually intense. The labia minora and atrophy in some cases disappear.

These conditions are illustrated in Figs. 5 and 6. I do not think that this atrophic condition is a terminal result of the hypertrophic condition but only another sign of lack of vitamin A and achlorhydria. One case (Fig. 5) has been found in a woman 27 years of age.

Infection of atrophic conditions. Infection in this type of case can also take place, but it is not so common as in the hypertrophic variety. It is usually a mild infection which has been caused by the patient who has scratched the already very atrophic skin. The skin becomes slightly reddened and is covered with small and very painful cracks.

Details of Case illustrated in Fig. 5, demonstrating atrophic condition.

Miss T., aged 27 years, had had vulval irritation for several years. She was also infected with trichomonas vaginalis. She was otherwise a healthy woman. On examination the skin over the vulva was white, shiny, and very thin. There were several small cracks and much greenish yellow discharge was issuing from the introitus. The urethral orifice demonstrated very well the red inflamed condition, which I have mentioned under the trichomonas vaginalis section of this thesis, as being typical of that infection. This point can be well seen in Fig. 5. The labia minora had completely atrophied although she was only 27 years of age, and the skin over the perineum was also thin and white. Her lips were very dry and cracked. A test meal showed no free acid, and she was put on acid and oil, and local treatment was not instituted for the trichomonas infection. She has improved immensely, and when last seen, on 2nd January 1936, was free from irritation. She is now able

to stand much more active treatment of the trichomonas infection owing to the very great improvement of the skin of the vulva.

Details of Case illustrated in Fig. 6, demonstrating atrophic conditions.

Mrs. B., aged 70 years, had had vulval irritation for only six months. She had no discharge, but was very tender over her vulva which had numerous cracks. She was otherwise a healthy woman who did not look her age. On examination the skin of the vulva was atrophied, thin, shiny, and white. The labia minora had disappeared in parts. She was given acid and oil and is improving.

Associated Cutaneous Lesions.

Various changes in the skin in other parts of the body can be demonstrated in nearly every case either of the hypertrophic or atrophic variety. These changes usually occur as a hyperkeratosis or thickening of the skin, and the commonest situation is the skin on the back of the hands and forearms. The skin takes on a darker colour, becomes the texture of chamois leather and loses its elasticity. This condition is well illustrated in Figs. 7 and 8, which were taken from the same case as Fig. 1.

Other cutaneous lesions noted were thickening of the skin on the neck and the alterations in the skin around the lips. Changes in the nails, which vary from simple ridging to the typical spoon-shaped nails, have often been noted. It is only during the last year that I have begun to look for these skin changes, and now that I know what changes may be present, I am finding some of them in nearly every case.

Symptoms.

The main symptom, and very often the only one, was intense irritation of the vulva, which was usually very much worse at night-time. In most cases the irritation was so bad that sleep was impossible, and in others the patients were awakened by the irritation and then found that they had been scratching the vulva. The duration of the pruritus had varied, but usually they had had irritation for years. Vaginal discharge was sometimes complained of, but indigestion was only occasionally mentioned. However, if the patients were questioned regarding both these symptoms, they were found to be present in quite a large number of cases.

Diagnosis.

The vulval lesions in typical cases have been illustrated, but these lesions vary from the very slightest thickening to the

types which cannot be missed. A test meal is always given to a patient who complains of irritation of the vulva whenever there is some form of thickening or whitening of the vulval skin.

It is most important that the vulva be examined very carefully in a good light so that any degree of whitening or shining of the skin can be noted. The labia should be pinched up between the fingers to note the thickness, consistence and elasticity of the skin and subcutaneous tissues. The epithelial tissues on other parts of the body should then be examined for signs of thickening, especially the skin of the back of the hands and forearms. The tongue should be examined for smoothness and the lips for cracks. The finger nails often show changes such as ridging and brittleness with a definite change in shape towards the typical spoon-shaped variety.

This condition of achlorhydria must not be forgotten in the patients whose vulvae are very much inflamed. Much time is often wasted by only treating the infection when the original cause could be treated at the same time. The event of an epithelioma developing in this condition should never be forgotten, and a biopsy should be done in suspicious cases.

Prognosis.

The progress of the condition can be arrested whether it be the hypertrophic or atrophic variety and the irritation can be relieved; in many cases the whole appearance of the vulva can be altered by treatment.

The improvement in the skin of the vulva and in other parts of the body is most noticeable, and the general condition of the patient usually improves at once due to the relief from the everlasting irritation. With the improvement in the vulval skin the risk of an epithelioma developing is greatly lessened.

Treatment.

Dilute hydrochloric acid is given by mouth, a teaspoonful to be mixed with a tumblerful of water. Half of this solution is to be sipped during the meal and the other half drunk after the meal. The acid is to be taken with each meal. It is most important that the acid be taken in this way.

If the acid solution cannot be tolerated, namely, the patient complains that it burns the throat, then further dilution can be used or the acid be taken in lemon squash. The acid must be taken for very many weeks; in fact, in a number of my cases

the irritation has at once returned when the patients have left off the acid, if only for a few days.

Cod-liver oil is also prescribed, a teaspoonful three times a day, or it is given in the form of hallivol. The normal diet in Australia contains plenty of vitamin A, but I have found that cases appear to improve more quickly if the oil is given.

Local treament in the form of a cream or paint is also prescribed to patients with very bad irritation. I have found a cream made of zinc oxide and starch with sweet oil of almonds to be most soothing. It can be cleaned off the vulva by wiping with more almond oil. In other cases a local anaesthetic ointment has been used, and I have found percainal ointment very useful. However, as soon as the patient had started taking acid the pruritus usually started to improve.

Any associated cause or causes should also be treated. The commonest associated cause in my cases was a vaginal discharge which was usually due to either an erosion of the cervix, infection of the vagina by the trichomonas vaginalis, or senile vaginitis. The general health of the patient should also be improved by the giving of iron and other tonics.

When infection has been superimposed on the hypertrophic or atrophic conditions, local treatment should be given for this, such as sitz-baths and the application of a soothing lotion; it is best to put the patient to bed. At the same time, however, the original cause, namely, the achlorhydria, should also be treated with acid.

I consider that X-ray treatment of the vulva should not be given, and that excision of the vulva should be reserved for the cases in which there is a very marked hypertrophy with a suspicion of malignant change.

Analysis of the 42 Cases.

Age. The ages of the patients varied from the youngest, aged 25 years, to the oldest, aged 73 years. In my series 23 patients had not reached the menopause, while 19 had passed either the natural or artificial menopause. This is very interesting, as in the past the conditions were supposed to start at or just after the menopause.

Duration of the pruritus. The average length of time during which the patients had suffered from irritation was about eight years. The longest time was 29 years and the shortest was three months.

Vulval condition. In eight cases the vulval condition had been noted as normal, but I feel sure that I should have noted some thickening or change in the skin if I had had at that time the knowledge which I now have as to the changes for which I ought to look. In the other 34 cases various changes were noted starting with a slight thickening to the very marked thickening and hypertrophy of all the vulval skin.

Test meals. Test meals were given in 35 cases, and in only four was the acid curve reported to be normal.

Four Cases of Normal Acid Secretion. Nos. 11, 12, 28, and 39.

Case No. 11 had the typical shiny vulval skin with other skin changes and typical nails. She improved very much on oil.

Case No. 12 had typical skin and nails, but as she was one of my first cases oil was not tried. Her vulval condition was very hypertrophic and she had been treated by various skin specialists, so I decided to remove the vulva. I saw her a few months ago and her general health has much improved on oil and acid. The operation had completely relieved the irritation.

Case No. 28 improved at once on oil after the discharge had been cleared up. She lived in Central Australia and her diet was not a good one.

Case No. 32 showed some improvement on oil.

One Case of Hyperacidity. No. 36.

Case No. 36 had a healed gastric ulcer with marked leucoplakic changes in the vulval skin with much thickening and whitening. She was put on oil and acid, as it was thought that perhaps the years of treatment with alkalis had upset the absorption of vitamin A and so caused the vulval changes and irritation. When last seen, on 5th February 1936, she was free from irritation.

Thirty Cases of No Free Acid or Low Secretors.

Actually there were 22 cases of patients who had no free acid and eight with low acid secretion. All the test meals were given by the same technician. Great improvement has been noted in 29 of these 30 cases, and one case has been lost sight of.

Seven Cases in which Test Meals were not given.

Although test meals were not given to these patients for various reasons, every patient was treated with oil and/or acid, and in every case marked improvement resulted.

In case No. 27 the indigestion, diarrhoea, and skin lesions were all improved by giving acid and the vulval irritation was at once relieved.

In case No. 30 oil and acid were given before the vaginal discharge had been treated and the irritation was at once relieved. The cervix was cauterized later.

In case No. 32 no improvement was noted until hallivol was given.

In every case improvement was noted after oil and acid had been given.

Associated Causes and Conditions.

In 23 cases discharge had also been present, and it was only after oil and acid had been given that the irritation was relieved, although in the majority of the cases the discharge had been cured.

Treatment.

Dilute hydrochloric acid has been given to every case even if the test meal showed a normal curve. In three cases, Nos. 12, 13, 31, excision of the vulva was performed with beneficial results, but each case was greatly improved after being given oil and acid at a later date. One of these, case No. 12, is now on acid, although she had a normal acid curve, and her general health has much improved. Case No. 13 had such a hypertrophic condition of the vulva that it was excised. She had no free acid, and is now taking acid with great improvement to her general health, and she looks years younger. Excision of the vulva did not completely relieve the irritation in case No. 21, and she was only relieved by taking oil and acid. She was achlorhydric. Perhaps the vulva need not have been excised in any case, and oil and acid might have cured them. Lately, oil has been given to every case, although I feel that the normal diet contained a sufficiency of vitamin A.

Treatment of the associated cause has always been carried out, such as electric cauterization of the eroded cervix and the local treatment of trichomonas vaginalis vaginitis and senile vaginitis. Iron and liver have been given to the anaemic cases.

Results and Remarks.

The improvement of the pruritus has simply been, in the majority of cases, miraculous. Patients who have had irritation for years have slept a normal sleep for the first time for years. Forty-two cases have been treated with oil and/or acid, and three also by excision of the vulva. I have been able to follow up 41 of these, and the irritation has been relieved in every case. One, No. 39, has not shown much improvement, but is very neurotic.

Summary and Conclusions.

1. Leucoplakia, kraurosis, neurotic pruritus, and atrophic vulvitis are various names which have been given to conditions which are the results of the same deficiency.

2. This deficiency is due to a lack of absorption of vitamin A, caused by a varying degree of achlorhydria.

3. A series of cases has been collected suffering from intract-

able pruritus with achlorhydria and other signs of a deficiency of vitamin A.

4. The addition of dilute hydrochloric acid to the normal diet of an Australian woman relieves the pruritus in the majority of cases with great improvement of the local vulval condition.

5. Vitamin A in the form of cod-liver oil should also be given.

6. It is suggested that the operation of excision of the vulva is not necessary in these cases except in those in which there is a suspicion of malignant change.

7. Epithelioma of the vulva should become increasingly more rare if this chronic irritation be relieved at an early stage by the giving of oil and acid.

8. This condition of achlorhydria is often present in cases of pruritus vulvae in which the irritation has not been relieved by curing the supposed primary cause.

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LIST OF CASES.

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
1.	4.5.35	B.	35	5 years	Thickening of subcutaneous tissues, atrophy of skin	Not done	Trichomonas infection, cracked lips	Previous hysterectomy; oil and local	Lives in Central Australia; greatly improved after oil; on 1.2.36 occasional relapse; otherwise very well
2.	12.7.35	B.	58	16 years	White and shiny thickening of skin and tissues of labia majora	Not done	Discharge for years; trichomonas infection; skin of neck thickened	Hallivol and local	Greatly improved after oil; general skin much softer; on 1.2.36 very well
3.	30.8.35	B.	28	2 years	Thickened skin	Low secretion	Erosion and discharge; indigestion	Cautery, oil and acid	No improvement after discharge cleared; much better after oil and acid; irritation recurs at times; on 22.1.36 no irritation.

LIST OF CASES (*continued*).

List of Cases (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
4.	4.7.34	C.	42	? years	Appeared normal	Low secretion	Erosion and discharge; trichomonas infection	Cautery, local and acid	Irritation returned February 1935, when acid relieved irritation
5.	1.8.35	C.	30	5 years	Appeared normal	No free acid	Gonorrhoea three years ago	Oil and acid	No irritation on 4.2.36
6.	22.6.31	C.	35	10 years	Thickening of tissues of introitus	No free acid	Slight discharge; small erosion	Acid	Some improvement, but the patient a neurotic wreck; not seen for three years
7.	21.10.31	C.	43	12 years	Leucoplakia	No free acid	Early pernicious anaemia	Acid, iron and liver	On 17.12.35 vulval condition perfectly normal; no irritation for 18 months
8.	4.7.35	C.	25	12 months	Thickening of skin with slight whitening	Very low secretion	Erosion and discharge; later trichomonas infection	Cautery; later oil, acid and local	No discharge but irritation still after cautery; later no irritation; on 11.12.35 relapse; had stopped acid; on 5.2.36 no irritation

List of Cases (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
9.	1.5.35	D.	44	9 months	Some thickening	No free acid; some acid after histamine	Erosion; indigestion; early greyness	Cautery, acid	No improvement after discharge cleared; on 7.8.35 no irritation after acid; on 11.12.35 no irritation and no indigestion
10.	1.10.35	D.	57	? years	Leucoplakia	No free acid	———	Numerous local applications for two years; later acid	Leucoplakia and pruritus unchanged for two years, then greatly improved after acid
11.	5.6.35	D.	55	10 years	Inflamed, sodden, white skin	Normal acid	Nails and skin; vaginal discharge	Oil and acid, local	Greatly improved on 1.10.1935
12.	6.5.31	H.	63	15 years	Leucoplakia with hyperkeratosis; very advanced condition	Normal acid	Skin and nails	Excision of vulva five years ago; acid and oil for one year	Pruritus much better; general health much improved after oil and acid

List of Cases (*continued*).

condition

List of Cases (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
13.	2.6.34	J.	64	20 years	Leucoplakia and hyperkeratosis; very advanced condition	No free acid	Skin; arms; hands	Excision of vulva and acid	Pruritus much better
14.	12.5.34	J.	28	3 years	Leucoplakia; spots on labia minora	No free acid	Erosion of cervix; tinea infection	Local, acid, oil, acid and oil	Neither local, acid, nor oil gave improvement of pruritus; acid and oil: irritation gone; married; on 1.2.36 some irritation
15.	7.1.34	J.	57	4 years	Thickening	Not done	Urethral caruncle	Local, acid and oil	Improved on 8.5.35
16.	20.6.34	J.	61	20 years	Leucoplakia; thickening of labia majora and whitening of skin over perineum	No free acid	Skin, arms, hands; indigestion	Acid and oil	Greatly improved on 23.1.35; on 13.12.35 no irritation; local condition much improved

LIST OF CASES (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
17.	27.3.35	L.	29	23 years	Normal	No free acid	Erosion and discharge	Cautery, acid	Greatly improved; pruritus returned when acid stopped
18.	27.3.35	M.	36	12 years	Whitened areas along labia minora; thickening	No free acid; no acid after histamine	Anaemic H.C. 50 per cent; erosion and discharge	Cautery, acid and iron	Better while taking acid and iron; irritation returned without acid and iron on 29.11.35
19.	13.11.35	M.	73	15 years	White thickening over labia majora and outer side of labia minora; corrugated and infected skin	No free acid	Senile vaginitis and discharge; skin on forearms	Local, oil and acid	Improving; on 1.2.36 no irritation
20.	31.7.35	M.	26	? years	Normal	Low secretion	Gonorrhoea	Local and acid	Pruritus did not stop after local treatment; much better after acid

LIST OF CASES (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
21.	28.4.35	Mc.	54	? years	Leucoplakia	No free acid	———	Excision of vulva; cod. oil and acid	Improved; on 31.1.36 irritation returned, not taking oil; on 10.2.36 irritation much better
22.	27.10.32	Mc.	32	15 years	Leucoplakia (very marked) with ulceration	No free acid	Glazed tongue	Oil and acid	At first greatly improved; relapsed on 1.7.35, taking acid incorrectly; on 12.2.36 improved
23.	1.5.34	Mc.	53	? years	Thickening	Not done	Indigestion; skin; senile vaginitis	Local treatment; hallivol	Improved greatly
24.	27.3.35	O.	30	5 years	White thickening of labia minora and labia majora	No free acid	Nails; indigestion	Acid and oil	Greatly improved; no irritation; general health much improved on 1.11.35

LIST OF CASES (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
25.	23.10.35	P.	64	29 years	White thickening of labia majora	No free acid	Skin; lips; nails	Acid and oil	Improving; irritation nearly all gone on 1.12.35; on 15.1.36 no irritation but must always take acid
26.	1.8.35	P.	25	4½ years	Normal	Low secretion	Eroded cervix; very fat	Thyroid and cautery; acid	No improvement after discharge stopped; greatly improved after acid; on 4.12.35 stopped acid; irritation returned
27.	1.10.35	R.	47	? years	Normal	Not done	Tongue; lips; nails; diarrhoea; indigestion	Acid	Irritation gone
28.	20.9.33	S.	33	? years	White thickening with atrophy of labia minora; very tight introitus	Normal acid	Some discharge	Local and oil	After years of local treatment no improvement at all; numerous treatments including X-rays; after oil no irritation; lived in C'tral Australia

List of Cases (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and condition	Treatment	Results and remarks
29.	1.8.35	S.	30	2½ years	Inflamed skin of labia	No free acid	Discharge and erosion	Cautery, acid	Not improved after discharge cleared; greatly improved after acid; on 15.1.36 no irritation
30.	1.5.35	S.	35	3 years	Normal	Not done	Erosion	Oil and acid, cautery	No irritation after oil and acid; later cauterized for discharge
31.	1.1.35	T.	27	4 years	White thickening with atrophy; no labia minora	No free acid	Trichomonas; lips; retroversion	Local, oil and acid	Gradual improvement of local condition and irritation; trichomonas infection very resistant; on 1.2.36 no irritation; vulva nearly normal
32.	1.2.33	T.	38	12 years	Whitened thickening	Not done	Trichomonas; indigestion; gastric ulcer	Local, hallivol	Had every treatment for years; on 1.10.35 no irritation after hallivol

LIST OF CASES (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
33.	17.5.35	T.	40	2 years	Atrophy	No free acid	Following radium for menopausal haemorrhage	Acid	No irritation on 5.2.36; general health much better
34.	—.8.32	S.	36	4½ years	Leucoplakic areas; some thickening	No free acid	Anaemia; thickening arms	Acid, iron and liver	No irritation; became pregnant; pruritus again in February 1935; not taking acid; put back on acid again and irritation relieved
35.	—.9.35	Mc.	41	4 years	Normal	Low secretion	Discharge; erosion; thickening skiin of neck	Cautery, oil and acid	Greatly improved; skin and general health much improved
36.	—.11.35	C.	54	20 years	Leucoplakia; thickening with ulceration	High secretion	Duodenal ulcer	Oil	On 5.2.36 irritation gone
37.	—.11.35	B.	72	6 years	Atrophy with cracks; shiny skin whitening	No free acid	Thickening of arms and hands	Oil and acid	On 22.1.36 no irritation

LIST OF CASES (*continued*).

List of Cases (*continued*).

No.	Date	Name	Age	Duration of pruritus	Vulval condition	Test meal	Associated causes and conditions	Treatment	Results and remarks
38.	—.11.35	H.	40	15 years	Atrophy; shiny skin of labia minora	Low secretion	Hysterectomy two years before for fibroid	Oil and acid	On 5.2.36 much better; relief for first time for years
39.	—.12.35	A.	47	14 years	Thickening of labia	Normal acid	Neck, face, arms; indigestion; total hysterectomy for fibrosis; senile vaginitis	Oil and acid	Senile vaginitis was cured; still pruritus; very nervy; on 5.2.36 some improvement
40.	—.12.35	C.	54	? years	Very inflamed; red weeping; much thickening	No free acid	———	Oil and acid	On 8.2.36 no irritation
41.	—.6.35	W.	33	2½ years	Reddened; slightly thickened vulval skin	No free acid	Anaemic 68 per cent; cracked lips; tonguesmooth	Acid and iron	On 21.12.35 no irritation
42.	—.12.35	D.	70	3 months	Labia minora; atrophic infection and cracks; thickening over clitoris	Very low secretion	———	Oil and acid	On 29.1.36 irritation much better

The Place of Induction of Premature Labour in the Treatment of Pelvic Disproportion.

BY

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INDUCTION of labour as a treatment for pelvic disproportion has particularly engaged my attention for the past two and a half years. During this time I have been in charge of the Rotunda Hospital, and have had unequalled opportunities of testing its value. I am satisfied beyond any doubt that it reduces the incidence of operative delivery, and any treatment leading in this direction must find an important place in the minds of those who are brought up in a conservative school. While no one will deny the value of Caesarean section and the obstetric forceps in certain cases of disproportion, it is most important that their use should be strictly limited and kept within narrow bounds.

There is unfortunately, at the present day, a marked tendency in the opposite direction. In many clinics, particularly abroad, Caesarean section has been allowed to assume an importance in obstetrics far beyond that to which it is entitled. Many writers and the reports of special committees have drawn the attention of the medical profession to the increasing incidence of the operation with its increase in maternal mortality. It is so relatively easy to perform and so often offers an easy way out of obstetrical complications that it is frequently resorted to, without due consideration of other methods of treatment, by operators whose knowledge of, and training in, the art of obstetrics is very limited. One must remember that it carries with it, even under the best conditions, a mortality which is at least three times as great as with vaginal delivery under all conditions. In addition, the unnecessary scarring of the uterus of a young primipara is a very unfortunate start in her child-bearing career. This is particularly so in Ireland, where sterilization is forbidden among Catholic women. As these form the great majority and as repeated sections up to five and six in number are by no means uncommon, it becomes increasingly important to avoid the operation with its consequent

dangers. I have in mind several cases in which a fatal termination followed the rupture of a uterus, weakened by previous scars.

In order to attain this end it is absolutely necessary to cut out all loose indications for the operation and to perform it only for those complications in which its use has been sanctioned by modern responsible obstetrical opinion. A study of the clinical reports of our important maternity hospitals leads us to the conclusion that there is no abuse of the operation among such units in the British Isles; a fact from which we may derive considerable satisfaction. It would appear, however, that undoubted differences exist between the Caesarean section rates of many of our leading clinics; in some centres it is three per cent or over, in others under one per cent. Local factors, such as a large number of emergencies or a high incidence of rickets among the population served by the hospital, will account for some of this difference, but it is necessary to inquire further into the causes of such discrepancies among hospitals in which similar conditions obtain.

A close investigation will reveal the fact that the incidence of Caesarean section depends considerably on the line of treatment which is adopted in cases of pelvic disproportion, particularly those in which there is a moderate degree of pelvic contraction. It will be seen that at those clinics at which only trial of labour at term is allowed have a higher Caesarean section rate than those at which the induction of premature labour is practised in the treatment of disproportion. I am an ardent supporter of the latter and I hope to prove my case by consideration of the results obtained by this method in the Rotunda Hospital. I will also endeavour to show that the maternal mortality and the foetal mortality have not increased from the adoption of this line of treatment.

During the years 1919 to 1926 the section rate in contracted pelvis was 0.43 per cent, and from 1926 to 1933 it was 0.79 per cent. In my first year it was 0.68 per cent and in the year just ended 0.34 per cent. From 1919 to 1926 there were 102 cases of induction for disproportion; these comprised 66 multiparae and 36 primigravidae; 10 infants were under six pounds and the remainder between six and eight pounds. There were nine stillbirths of which six occurred during the last two years of this period when some unsuitable inductions were tried: 79 cases ended spontaneously, 15 in delivery with the forceps of which in four the head was in the middle strait, three ended in pubiotomy and two in Caesarean section. There were three cases treated by podalic version which accounted for three dead infants. These were really

unsuitable cases for induction and should have been left until term for section. Labour was induced in all the cases between the thirty-seventh and the fortieth weeks, and all the multiparae gave evidence of previous difficult deliveries with stillbirths after breech labours, delivery with the forceps, or craniotomy: nine had had previous pubiotomy and three previous Caesarean section performed for disproportion; there was one maternal death in the series.

During the next seven years there were 151 inductions for disproportion with 10 stillbirths, of these seven ended in Caesarean section and three in pubiotomy, the remainder were delivered spontaneously or with forceps. During my two years there were 33 cases of disproportion treated by induction of labour with one foetal and no maternal death. Of these 18 ended spontaneously, six by Caesarean section, one by pubiotomy and the remainder by delivery with the forceps. The majority of these were cases of definite pelvic contraction with a conjugata vera of nine centimetres or less. Thus during this time there were, in all, 286 cases of disproportion treated by induction of labour with one maternal death and 20 foetal deaths. This foetal death-rate of 7 per cent does not compare unfavourably with the average general rate of 5 or 6 per cent.

In order to successfully practise induction of labour as a treatment of disproportion there are certain rules and regulations to be observed. In the first place it should never be performed before the thirty-seventh week, as before then the infant is too premature to have a reasonable chance of survival. Secondly, generally speaking, it should not be performed if the conjugata vera is less than 8 centimetres in a flat pelvis, or 8.5 centimetres in a generally contracted pelvis. It should not be attempted in an elderly primigravida with a small pelvis. Thirdly, an extremely careful and accurate examination should be carried out under an anaesthetic, in order to determine the right time to induce premature labour. This can only be learnt from long experience; at first many errors of judgment will occur, in some cases premature labour will be induced unnecessarily, the patients would deliver themselves at term if left alone; in others premature labour will be induced too late, necessitating operative delivery. The ideal of induction is to procure a spontaneous, easy labour two or three weeks before term in a woman who would have had dystocia at term. The infant should weigh at least 6 pounds. As 7 or 8 ounces is an average weekly increase during the latter weeks of pregnancy, it will be realized how valuable the method can be.

This ideal cannot always be attained and I do not see any objection to inducing labour in a border-line case at the thirty-seventh or thirty-eighth week and giving a trial of labour. If such a trial fails I am not perturbed at having to perform a lower segment Caesarean section. I have not had any deaths, and there has been very little morbidity in such cases. It is essential, however, that the induction should be carried out with most rigid asepsis, and subsequent vaginal examinations should be reduced to the minimum. It is also necessary that the membranes should remain intact as long as possible and, therefore, puncture of the membranes should not be employed as a method of induction; it is a most unsatisfactory method when the head is high and prevented by the bony pelvis from sitting down into the lower uterine segment. I employed it in several of my early cases and found myself driven by want of proper labour and the occurrence of early foetal distress, into what one might aptly term, sentimental Caesarean section. Had proper labour supervened spontaneous delivery would probably have taken place. If the patient is at, or near term, medicinal methods should be tried. These, however, are unsuitable before term as they are unlikely to succeed and much valuable time may be lost; with the rapid increase in weight of the child the optimal time for induction may be passed. If such measures fail, or are unsuitable, the insertion of three gum elastic bougies or a stomach tube into the lower uterine segment will be best. Both methods are fairly successful and there is little to choose between them. The instruments should be left in the uterus from 36 to 48 hours and then withdrawn if labour has not started. Twelve hours later they should be reinserted following preparatory stimulation of the uterus with castor oil and quinine. Should labour start they must be left in until good strong pains occur and the os has reached a quarter to half dilatation. It sometimes happens that the placenta is separated slightly from its attachment by either the stomach tube or bougie and a sharp haemorrhage results. The instrument should be withdrawn at once, when the haemorrhage will usually cease. This accident can be avoided by changing the direction of the bougie or stomach tube if an obstruction is encountered. Instrumental induction may occasionally be followed by irregular uterine action, giving rise to early rupture of the membranes and uterine inertia. Such cases are, however, uncommon and would probably exhibit the same malfunction had labour started spontaneously. As mentioned above it is a very important thing not to induce with too small an infant. One should endeavour to esti-

mate by palpation the approximate weight of the child. With practice it is possible to arrive at a margin of error of half a pound or less. Babies of 6 pounds, or over, provided they are not exposed to a difficult labour, can be relied upon to do reasonably well. If it is felt that the pelvis will not accommodate a child of this weight, it is better to leave the case until term for Caesarean section.

The choice of suitable cases is made as follows:

In the first place we keep a careful lookout for all women who appear to have reached, or gone over, term with large babies; we induce labour in any who give evidence of the least disproportion. This is a very important advance in modern obstetrics, and a cursory glance over the records of a previous generation will reveal the great amount of dystocia which arose from post-maturity and infants with large hard heads. Last year in the Rotunda Hospital labour was induced in 150 cases at, or after term, chiefly by medicinal methods when it was thought that the infants had reached a sufficient size.

Secondly, we pay particular attention to multiparae with histories of previous dystocia, such as difficult delivery with the forceps, stillborn breeches, and craniotomies. The patients are warned to attend the antenatal clinic during pregnancy and are sent into hospital for a thorough investigation at the 36th or 37th week. Finally, all primigravidae who present any sign of disproportion or contracted pelvis, such as small external measurements, unfixed head, malpresentations, pendulous abdomen or signs of rickets, are sent into hospital at any time between the thirty-sixth week and term. This also applies in cases in which the head cannot be pushed into the brim of the pelvis by the external Müller's method. A careful assessment of the size of the pelvis is then carried out. This is done as follows:

(*a*) Careful external and internal pelvimetry. I believe that external pelvimetry should be done as a routine because it will often draw attention to a contracted pelvis, especially if of the flat rachitic type. Internal pelvimetry will give definite information as regards the size, and particularly the type, of the pelvic brim and, in my opinion, is a very useful help in forming an opinion as to the prognosis for delivery. The knowledge of reasonable internal diameters has often encouraged me to carry on a trial of labour to a successful issue when other factors had suggested a failure.

(*b*) A careful investigation of the interior of the pelvis under anaesthesia and an accurate estimate of the fit of the head into the

pelvic brim by the internal Müller-Kerr method. Information of value cannot be gained without anaesthesia except in those cases in which there is absolute disproportion or none at all. In the border-line cases it is only possible to gauge the part played by the soft tissues and the extent to which the head can be pushed down into the brim, when the patient's abdominal muscles are properly relaxed. If the breech is presenting, the foetus should be turned by external cephalic version and a day or two allowed for it to settle down before further investigation. In multiparae all previous information as regards the weight of the baby, and the nature and length of the labour, is carefully taken into consideration.

The patient is anaesthetized and is turned into the dorsal cross-bed position and her legs are held by assistants. The vulva is carefully washed, the vagina is douched, the bladder is catheterized and a sterile towel is placed upon the abdomen. Two fingers of the gloved hand are introduced into the vagina and the difficulty or ease with which the promontory of the sacrum can be reached is determined. If easy to reach the pelvis is flat; if the promontory is high difficulty is suggested, as the increased slope of the plane of the brim makes it harder for the head to engage. The brim is palpated all round with the fingers. Normally it is difficult to reach the posterior third. Particular attention should be paid to the back of the symphysis pubis and often a projecting boss of bone is found to be present in this region. This sometimes has the effect of reducing the length of the conjugata vera by 0.5 to 1 centimetre and may prevent proper engagement of the head. Next the sacrum is felt; it should present a concave surface from above downwards and from side to side. It is often flat or even convex in its upper part in rachitic pelves. Occasionally a false promontory at the junction of the first and second and that of the second and third pieces of the sacrum will be noticed. This may considerably reduce the antero-posterior diameter. The sub-pubic angle is next measured with the fingers and the size of the pelvic outlet, particularly the posterior sagittal diameter, is estimated. Fortunately contraction of the outlet is rare in Ireland. This survey will give a good idea of the type of pelvis with which one is dealing. Internal pelvimetry is next carried out with a Skutsch pelvimeter and after some practice quite accurate results can be obtained. I have several times been able to confirm my measurements by direct mensuration of the pelvic brim at Caesarean section. The lengths of the conjugata vera and transverse diameters must be carefully

considered and it should be borne in mind that it is possible for the head of a baby weighing 6½ or 7 pounds to come through a pelvis with a conjugata vera of 8 centimetres provided there is plenty of room in the transverse diameter. A small round pelvis with measurements of, say 9 centimetres conjugata vera, and a transverse diameter of 9.5 or 10 centimetres, which is quite a common type, has not such a good prognosis for delivery.

The next step is to carry out a careful internal Müller-Kerr estimation of the fit of the head into the pelvis. Two fingers of the right hand are placed into the vagina and the thumb over the front of the symphysis pubis; the head is grasped by the left hand by the reversed Pawlik's grip and pushed downwards and backwards past the promontory of the sacrum in the direction of the brim of the pelvis. At the same time one endeavours to keep the head flexed so that the vertex presents—this is an important consideration. An assistant now pushes strongly on the fundus uteri so as to push the child towards the pelvic brim; this pressure should not be retained for more than 30 to 40 seconds at a time. It will now be possible to estimate how far the head can be pushed into the brim, or failing that, how much it overrides the brim. I am in the habit of recognizing and teaching five degrees of disproportion.

Degrees of disproportion. (1) The head can be pushed on to the pelvic floor; there is not any disproportion and this type should be recognized by Müller's external method without anaesthesia. The patient can be allowed to go to term.

(2) The head can be pushed as far as the ischial spines; this indicates that there is not any disproportion but there is not the normal amount of reserve space between the brim and the head; the case should be re-examined in 10 or 14 days' time. It must be remembered that the infant itself gains 7 or 8 ounces per week *in utero* during the last four or five weeks and its head gets bigger and more ossified. A case of this type discovered about the thirty-seventh week would be suitable for induction at the thirty-ninth week and should certainly not be allowed to go over term.

(3) The head can be pushed into the brim but not through the brim; overriding is not felt by the thumb on the symphysis pubis but there may, however, be slight overriding of the brim at the ends of the transverse diameter as felt by the fingers in the vagina. This is a case of disproportion with a good prognosis for vaginal delivery if labour is induced within a few days' time. Uterine action and moulding should easily suffice to overcome the discrepancy in fit.

(4) The head can be made to bite the brim but cannot be pushed into the brim. On palpation with the thumb of the vaginal hand the anterior surface of the head will be found to be almost flush with the anterior aspect of the symphysis pubis or may even slightly override it. The internal measurements will point to a small round pelvis with a conjugata vera of 9 centimetres or less, or to a flattened pelvis with a conjugata vera in the neighbourhood of 8 centimetres. The longer the transverse diameter the better is the outlook. The prognosis for vaginal delivery is doubtful but it is always worth while finding out what can be done with such a pelvis. Labour must be induced at once and a long and carefully watched trial carried out. It is in this type of case particularly that Caesarean sections are saved. One is often surprised through how small a pelvis a baby weighing 6 pounds 8 ounces, or 7 pounds, will sometimes pass. If one conducts the trial of labour in the proper way and learns to recognize as early as possible the signs which indicate failure of mechanism then Caesarean section can be undertaken without any fears or qualms of conscience. I have performed seven lower segment Caesarean sections in such circumstances; only one of the patients developed a minor degree of puerperal pyrexia. In several of these cases the membranes had been ruptured for 24 to 36 hours. The alternative in this degree of disproportion is Caesarean section at term, and it has always seemed to me worth while to take the chance with induction if the infant is a reasonable size. As mentioned above many of the infants will come through and in those which fail to come through there is a safe way out of the difficulty. A most important consideration is the valuable information which is gained regarding the capabilities of the pelvis in these patients, and this can be applied in their subsequent confinements.

(5) The head cannot be pushed into the brim at all and on palpation with the thumb the front of the head will be found to be considerably overriding the front of the symphysis pubis so that the passage of the thumb upwards is completely arrested. In such a case the head will be very high or may actually be displaced into one or other of the iliac fossae. The measurements of the brim will indicate a severe degree of contraction with a true conjugate diameter probably of 7 centimetres or less. This is a case of absolute disproportion and the only treatment to be considered is classical Caesarean section at term, or when labour begins. The lower segment operation is not suitable at the beginning of labour as the lower segment is still unformed. Cases such as these can often be diagnosed without an anaesthetic.

At the end of this investigation one will have decided whether to induce and when to induce, the ideal being to procure a reasonably easy labour for an infant whose size and maturity are such as to ensure a good start in life. The argument has been advanced that induction is often performed unnecessarily. The more experience one has the less likely is this to happen. Besides, it is of no great consequence if it does sometimes happen if one does not produce an infant of less than 6 pounds. My morbidity-rate in cases of induction for the past two years was 4 per cent, so from this point of view it is not contra-indicated. Many cases as explained above, do not come into the ideal category and are border-line when first seen at the thirty-seventh or thirty-eighth week. Labour should be induced in these and given a trial. The management of this trial of labour requires careful consideration. The same remarks will apply to trials at full time. A most important point is that the doctor should be in close and constant touch with the case so that he can observe it carefully—such a position obtains at the Rotunda Hospital where the Master lives on the premises. In such cases, which may at first appear to have a bad prognosis, the patients will often deliver themselves if given time. The temptation to interfere is more likely to be avoided by the doctor who is within easy reach of the case.

Management of a Trial Labour.

After labour has begun the patient's abdomen is carefully palpated and the position of the head as regards flexion and the height above the brim is noted. Narcotics may be given during the first stage, particularly if the patient is nervous. Some 8 to 10 hours later the head is again palpated and attention is paid to two points. (*a*) Has the head descended? (*b*) Has flexion been maintained? A rectal examination may also be carried out to ascertain the size of the os and the amount of bulge of the membranes. In a favourable case the membranes will remain intact and continue to dilate the cervix, the head will maintain its flexion and descend into the brim. In an unfavourable case the membranes will rupture early and if this is accompanied by extension or asynclitism of the head the prognosis is unfavourable. It is then better to decide at once on Caesarean section. If early rupture of the membranes is accompanied by maintained flexion of the head it is right to continue the trial and sometime later a second rectal examination should be made to ascertain the condition of the cervix. If the cervix has continued to dilate and is well applied to the presenting part the prognosis is good, because the bony pelvis

has allowed the head to descend and take the place of the membranes as a dilating force.

If the cervix has not continued to dilate or has actually reformed again and is not well applied to the head the prognosis is bad and vaginal delivery is unlikely. It is important to recognize these unfavourable signs as early as possible after rupture of the membranes in order to decrease the risks from Caesarean section. So long as the head remains in good position, the os continues to dilate and there are not any signs of foetal or maternal distress, it is rational to carry on the trial of labour. Spells of 20 to 30 minutes in Walcher's position may be tried with effect. If the uterine action remains efficient the head usually moulds slowly through the pelvis and comes down on to the perineum. If not born spontaneously in a short time the forceps should be applied to effect delivery as it is not advisable to subject the patient to further effort or the foetus to further pressure. When the head has moulded through a rachitic flat pelvis the rest of the labour is often quick, as such pelves are characterized by wide outlets.

If the cervix continues to dilate but the head ceases to make progress it will be well to carry out a careful vaginal examination after 10 or 12 hours of good labour. This will be necessary earlier if foetal distress arises. In such cases Pawlik's grip will often convey an impression of fit behind the symphysis, but on careful palpation at the sides it will be felt that a good deal of head is still above the brim. This is likely to obtain in generally contracted pelves, and in generally contracted and flat pelves, and will sometimes arise in cases of the fourth degree mentioned above. The patient should be anaesthetized and after careful preparation the size and condition of the os, the lie of the head and the amount of moulding and caput should be investigated. If there is marked moulding with overriding of the parietal and occipital bones, and if the anterior lip of the cervix is long and oedematous, it will usually be found that the greatest diameter of the presenting part is still above the brim. In such cases vaginal delivery is not to be hoped for and it will be best to treat the case by lower segment Caesarean section. In my opinion there is no need to fear the operation if the trial of labour has been carried out as outlined above. One has the satisfaction of having given the patient every chance of vaginal delivery and of having gained valuable information for the next confinement.

In a more favourable case than that just described the os will

be fully, or practically fully, dilated and the head will be lying in the brim of the pelvis. There may be some apparent asynclitism, which is, however, often due to moulding. There may be exaggrated flexion suggesting a generally contracted pelvis. Nature has just failed to overcome the disproportion. This is a case in which tentative, but only tentative, delivery with the forceps should be tried. The operator should sit on the floor or low stool and, with the patient in Walcher's position, make traction in the axis of the brim and upper middle strait. Only a moderate and controlled force should be applied for a short time and, unless the head comes readily down, one should desist from further effort. If failure ensues one is now faced with two alternatives, Caesarean section or pubiotomy. It is not feasible to allow further time for moulding as the mother and infant are becoming distressed. Caesarean section is the operation usually selected at this time, but in my opinion we now have the proper indications and the proper type of case for the operation of pubiotomy. That is to say, the os is fully dilated, the disproportion is not too excessive and the foetus not unreasonably distressed. It is at this time a safer method of delivery than Caesarean section and is a method of escape from the results of a too optimistic prognosis. The vagina is douched, the bladder emptied of all but one ounce of urine, and either Bumm's or Döderlein's needle passed on the left side, about three-quarters of an inch from the pubic symphysis. Great care must be taken that the weight of the legs is lifted off the pelvic girdle until delivery is effected—this is a most important precaution. As soon as the needle is in position the remaining ounce of urine is withdrawn from the bladder to make sure that it is not blood-stained by injury. A Gigli saw is attached to the hook on the needle and drawn into position. The bone is then divided. The head is pushed from above down into the enlarged pelvis, the forceps is applied and the child extracted. The divided bones will separate sufficiently to allow easy passage of the head. It is not advisable to wait for spontaneous delivery after pubiotomy. The placenta is expressed as soon as it has left the uterus, the legs are brought carefully together, and three or four long pieces of elastoplast are applied across the pelvis from one thigh to the other. The patient is encouraged to sit up in bed from the second or third day, she gets up on the tenth day and walks on the twelfth day. She is usually able to leave hospital by the end of 15 or 16 days. One desires to get fibrous, not bony, union, and that is why early movement is encouraged. A slight permanent enlargement sometimes results. I have performed six

pubiotomies in such cases during the past year and none of the patients gave cause for anxiety at the time of operation or during the puerperium. X-ray photographs were taken in all cases and showed the bones in reasonably good apposition. There was a slight difficulty in walking and stiffness in the left leg for a few days in some of the cases, but this soon disappeared. I have sent a *questionnaire* to all these patients three or four months after the operation and they all reported themselves able to walk quite normally. I have seen and examined three of them; the ends of the bone seemed to be in good position and the patients were able to walk without any trouble whatever. There was not any injury to the bladder or subsequent sloughing of the tissues in any of the cases. Four of them had vaginal tears in the left fornix owing to the loss of bony support during the time of delivery, but these healed well without stitching. Pubiotomy has been performed in the Rotunda Hospital for the last 25 years, and with excellent results, so long as its performance was limited to the type of case mentioned above. I do not wish it to be thought that I consider pubiotomy a desirable ending to induction of labour, I merely wish to indicate that it is always worth while inducing labour in a border-line case to save Caesarean section. If a mistake is made and the disproportion is a little too great pubiotomy can be resorted to as a way out with the knowledge that it is a safer operation than lower segment Caesarean section.

Induction of labour is of special value in multiparae with previous dystocia and it should be carried out at the thirty-ninth or fortieth week in normal multiparae who tend to overcarry and have large babies in their later pregnancies. The truth of this remark has been abundantly proved in the Rotunda Hospital Clinical Report for last year. We had 15 cases of difficult deliveries with the forceps; five of the patients had not received antenatal care, had gone over term and been delivered with the head in the middle strait of the pelvis with the forceps, of babies of 9 pounds or more. In women with many pregnancies it is possible that there is a calcium depletion which tends to alter or reduce the size of the pelvis and to interfere with the efficiency of the uterus. It does not follow that because a woman has delivered herself of a normal full time infant that she will necessarily do so in each successive confinement.

I have endeavoured to make the case that induction of premature labour will reduce the incidence of Caesarean section; a study of hospital statistics from different clinics will prove this to be so. To quote from the clinical report of the Coombe Hospital

for the year 1935: "During last year we reduced the number of cases of induced labour. As a result . . . there has been an increase in the number of forceps cases and of Caesarean sections. We are, therefore, confirmed in our former opinion that in pelvic deformity of minor and upper medium degree induction of labour should be carried out." If this treatment for disproportion is carried out with due regard to its limitations no harm will result to mother or child. Caesarean section is on the increase—a fact which must give rise to anxiety amongst thoughtful obstetricians. Let us endeavour to curb this tendency by practising and teaching the principles which I have adopted as the theme of this paper.

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The Treatment of Amenorrhoea and Kraurosis Vulvae with the Follicular Ovarian Hormone.

BY

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MANY medical men are now familiar with the fact that the ovarian follicular hormone, oestrin, is applicable to the treatment of menstrual and climacteric disorders. The chief clinical work on this subject has been done by Kaufmann[1] in Germany and Cassidy and Kurzrok[2] in America.

I have been working for the last 18 months with the most potent form of oestrin which has yet been prepared—that is, oestradiol benzoate, which is the benzoic acid ester of dihydroxy-oestrin. This ester, which is dissolved in oil, has been shown to produce a prolonged action only necessitating bi-weekly intramuscular injections. These injections are supplemented by giving four times daily small oral doses of a mixture of dihydroxy-oestrin and ketodroxy-oestrin dissolved in naturally occurring lipoids, in the form of dragées of 1,000 international units each.

The follicular hormone preparation which I used was Progynon B. Oleosum, which is put up in two strengths for intramuscular injection in ampoules of 1 c.c. containing 10,000 international benzoate units (I.B.U.), equivalent to 1 mg. of oestradiol benzoate and 50,000 I.B.U. equivalent to 5 mg. of oestradiol benzoate.

In this short paper I am giving my results on the treatment of two important disorders of women, the one associated with the period of sexual activity and the other following the cessation of function of the ovaries: (1), amenorrhoea, and (2), kraurosis vulvae.

1. *Amenorrhoea* is subdivided as follows:

(*a*) Primary amenorrhoea: (i) With hypoplastic genitalia; (ii) with normal genitalia.

(*b*) Secondary amenorrhoea. (i) Cessation of cyclical uterine bleeding following normal regular menstruation; (ii) Cessation

of cyclical uterine bleeding when previously menstruation has been irregular with gradually lengthening intermenstrual intervals.

2. *Kraurosis vulvae* is essentially an atrophic condition of the vulva usually following the menopause and, therefore, seen in women of 43 to 60 years of age, or in younger women from whom the ovaries have been removed. Berkeley and Bonney describe kraurosis as "an atrophic condition of the vulva associated clinically with stenosis of the vaginal orifice, and pathologically with certain changes in the dermis."

PHYSIOLOGY.

(*a*) *Primary amenorrhoea* is a condition not very much benefited by this therapy, the idea of which is to stimulate the growth of the whole uterus, both myometrium and endometrium, and thereby to prepare the field for the action of the patient's own follicular hormone. The fault, however, may be due to one of two things: (*a*) failure in the pituitary-ovarian mechanism, or (*b*) an inherent defect in the Müllerian duct system.

Kaufmann[2] has succeeded in producing menstruation in a few cases, using oestrin and progesterone in patients with normal genitalia, but there was no continuance following cessation of treatment.

Doses in the region of 4,500,000 I.B.U., or 450 mg. of oestradiol benzoate are given in eight to ten months.

My one case, a girl of 20 years, with a unicornute (?) uterus, was given gradually increasing doses, and in a period of eight months received 4,020,000 I.B.U. and daily dragées. After only 100,000 I.B.U. in a month bleeding was seen for two days. Nothing, however, has occurred after this, even with the big doses. (Case No. 22).

(*b*) *Secondary amenorrhoea.* In very many cases the history will relate some physical or mental shock, change of outlook, or conditions of life. Although there is no direct physiological evidence for the theory of Hohlweg and Junkmann[3] that the pituitary gland is controlled by nervous impulses from the hypothalamus, clinical evidence is strongly in its support, and in these cases probably the ovary is not so much at fault as the pituitary —the controller of the ovarian cycle.

From physiological data it is thought that injection of oestrin has a reciprocal stimulus on the pituitary apart from its proved action on the uterine endometrium and accessory genitalia.

Treatment.

Treatment of secondary amenorrhoea is thus based on an exact reproduction of the normal female cycle, so far as we are acquainted with this function. The essential points to bear in mind are:

(1) That the menstrual cycle is divided into two phases: (*a*) The proliferative phase, which is controlled entirely by the follicular hormone—oestrin—which, we believe, is produced in increasing amounts by the granulosa cells lining the Graafian follicle. This process lasts on an average 12 to 17 days, and during this time there is a steady growth of the columnar-celled glands of the endometrium and the stroma becomes very vascular. (*b*) The secretory phase. Schroeder[4] has shown that round about the fifteenth day of the average normal cycle the glands start to become convoluted and rapidly become secretory. All glands are in full secretion by the end of 21 days, and these changes are even more marked in the fourth week.

This change in the endometrium is brought about by the action of the corpus luteum hormone—progesterone—which only influences the endometrium after a sufficient amount of follicular hormone is produced.

Normally the change from proliferation to secretion is controlled by ovulation, which is thought to take place around the thirteenth day after the cessation of the last menstrual period; or, perhaps more accurately expressed by Knaus,[5] ovulation occurs 15 days counting back from the first day of the next menstrual bleeding. This may explain the cycle of five to six weeks in which the proliferative phase is lengthened, possibly due to an increased size in one follicle before rupture, or the maturation of two follicles of not quite the same age.

(2) That the menstrual cycle is essentially a rhythmic phenomenon governed primarily by the anterior pituitary hormone—Prolan.

Jeffcoate has shown that menstruation occurs physiologically from the proliferation phase of the endometrium in 25 per cent of cases, and says that in these ovulation does not occur—the bleeding is described as non-ovular menstruation.

Therapeutically Kaufmann has shown that bleeding will occur from a proliferation phase artificially produced from 5 to 13 days after cessation of injections of oestrin, with which result I agree, and I have produced bleeding in this manner from the endometria of women who have had their menopause 5 to 19 years previously.

It is well known that normal menstruation usually occurs following the sudden cessation of progesterone due to the atrophy of the corpus luteum, which occurs cyclically unless the ovum is fertilized.

When treating a case of secondary amenorrhoea, therefore, one has to consider the nature and possible resistance of a case to treatment. The duration is of little real importance, it can practically be guaranteed to start bleeding by progynon treatment if adequate dosage is given; but one has to consider the best and quickest means of re-establishing the cyclical rhythm.

Mild cases will only need supplementary therapy with doses such as 10,000 I.B.U. bi-weekly, whereas the long-standing cases may need complete substitution therapy in doses found by Kaufmann in his work on women from whom the ovaries have been removed to be suitable for the production of endometrial proliferation, i.e. 250,000 I.B.U. given in doses of 50,000 I.B.U. bi-weekly. Possibly even greater doses than these may be required.

The application of this therapy is the next important matter. Cyclical rhythm may be started at once in cases of short duration. By this I mean five injections of 10,000 I.B.U. are given at intervals of four days on the first, fourth, eighth, eleventh, and fifteenth days. If bleeding has not started by the twenty-eighth day another five injections of 50,000 I.B.U. are given at intervals in the next 15 days, and probably bleeding will start on an average seven days after the last injection, according to my figures.

Immediately bleeding has ceased once again a proliferation phase is built up by repeating five doses of 50,000 I.B.U. in the first 15 days of the established cycle.

Gradually the dose, which has been found by trial to be adequate for production of a normal menstrual loss, is lessened, thus for the next course two doses of 10,000 and three doses of 50,000 I.B.U. may be given, and then three doses of 10,000 and two doses of 50,000 I.B.U., and, finally, five doses of 10,000 I.B.U.

In each case it is suggested that oral doses should be given to maintain the low, steady oestrin level throughout the cycle, four dragées each of 1,000 international units being swallowed daily before food. After the cessation of injections a course of these dragées may be alone given for 15 days.

In this way cyclical menstruation may be re-established, but probably once it is started, it should be maintained for about

four to six months by the smaller intramuscular doses to re-educate the pituitary-ovarian mechanism.

Follicular hormone therapy alone is certainly satisfactory and able to induce bleeding in some cases from endometrium in the secretory phase. In these patients we can imagine either that the natural oestrin was inadequate for formation of a corpus luteum or else that reciprocal stimulation occurs via the pituitary.

Results.

Twelve patients with secondary amenorrhoea of duration from six weeks to 24 months have been treated; seven were single and five were married. Menstruation prior to amenorrhoea was regular in six and irregular in six. All the patients complained of some symptoms apart from the absence of menstruation, such as langour and depression, obesity, sterility, or even mental retardation.

Treatment varied from 450,000 I.B.U. in five weeks to 1,790,000 I.B.U. administered in 40 weeks. All patients commented on an increase in vitality, most marked in those who were previously languid and tired or depressed. There was not any appreciable alteration in weight, and one patient who was sterile is still sterile.

Menstruation was produced in all cases but one,* and was in regular monthly cycles during treatment in all those patients who were able to attend regularly.

Regular spontaneous bleeding after cessation of treatment has occurred in one case so far. Two failed to follow-up. There was not any spontaneous bleeding after cessation of treatment in two cases. The other patients are still continuing treatment and conclusive results cannot yet be drawn up.

In two cases rhythmic bleeding restarted after a latent interval; in one case eight months and the other three months after stopping injections.

Kraurosis Vulvae.

One of the most promising fields for oestrin therapy is the climacteric, and I do not know of any drug or combination of drugs which is so potent and so specific for climacteric disturbances as oestrin.

Flushes and hot sweats are gradually improved, lessened

* This one refractory patient has since menstruated after the great dose of 2,000,000 I.B.U. administered in 60 days, followed by a period of six days free from injections.

both in frequency and severity, and soon are kept completely in abeyance. Psychic depression, praecordial pain and its associated anxiety (in the absence of organic disease) and pruritus vulvae are all symptoms which the general practitioner sees perhaps more often than the gynaecologist. These react with remarkable rapidity to adequate oestrin therapy.

In this short paper I am only dealing with kraurosis vulvae, since it is a severe and otherwise intractable condition. Kaufmann started treating his cases in 1934, and I first attempted treatment in January 1935. In a period of 14 months I have had eight cases under observation and the results are encouraging. The age of the patients varied from 45 to 67 years, the menopause having occurred from 6 to 17 years previously, and the onset of severe irritation or other major symptoms started any time from the menopause till 17 years after.

The Theory of Oestrin Therapy.

Physiological experiments show that oestrin has a marked action on skin, and in particular on skin and mucous membrane of the genitalia, where it causes an increased growth of squamous cells and hyperaemia of the deeper tissues.

Application.

As the cyclical process is not going on in the climacterium, injections may be continued bi-weekly until the condition is relieved and dosage is then gradually reduced. I have found that the best way to obtain a quick result for the relief of the patient's symptoms is to give massive doses of progynon from the start. I began treatment of my first case with bi-weekly injections of 50,000 I.B.U., and although it was not a severe case, treatment had to be continued for 44 weeks. Relief was obtained after six weeks, and this patient had two relapses.

After this I began by giving doses of 200,000 I.B.U. or 250,000 I.B.U. twice weekly, and found that relief was obtained in two and a half weeks in my next case, which was more severe. The dosage was then gradually lowered, and 10,000 I.B.U. is being given once weekly to this patient for a few weeks, and, finally, dragées only will be given for about 14 days.*

* A further advance in this therapy has been obtained by the vaginal application of oestrin in oil, in the form of gelatin-coated capsules of 3,000 international units, which were specially made by Schering Ltd. These are now being used instead of dragées by mouth.

A feeling of well-being is usually noticed by these patients, possibly due directly to oestrin therapy or else as a result of having relief of their intolerable irritation and soreness.

One must be prepared to give not only large doses, but they may have to be continued for a long time and very gradually reduced. If irritation recurs at any time, the minimal dose effecting relief must be maintained for a while longer.

Colour changes, while intense therapy is being maintained are not noticeable, but fading or even disappearance of the vestibular redness is noticed as soon as the dose is diminished.

Colour photography by the Dufaycolor process has been used to compare results before and after treatment. Care, however, must be used to standardize the technique as much as possible. The method is not of routine use owing to the expense.

Dosage to the point of saturation is probably required before relief can be expected quickly. In three cases I took the urine of patients having 250,000 I.B.U. and 200,000 I.B.U. bi-weekly and had carried out with each an experiment using the technique of the Aschheim-Zondek test. In all these cases I saw that there was marked hypertrophy in the uteri of the mice and no ovarian changes. When dosage was reduced, so also was the size of the uteri of the test mice. To obtain a rough idea of the excretion dosage in the patient's urine four mice were each given one dose by injection of 2,500 I.B.U. progynon, and after five days the hypertrophy of the uterus was about twice as much as in the clinical experiments. Even a mouse, who lived in the same cage as the injected littermates showed marked hypertrophy of its uterus, no doubt due to its food having been contaminated with the urine of the other mice.

Results.

Eight actual cases of kraurosis vulvae were treated—all married women. Two lived many miles from Bristol and could not continue treatment sufficiently for a complete cure. All patients who attended regularly and received adequate dosage were benefited.

In the early cases, as in cases of pruritus, bi-weekly injections of 50,000 I.B.U. were given over a long period with good success. The later cases, which incidentally were very severe, were treated from the beginning with injections of 200–250,000 I.B.U. bi-weekly with more rapid relief and less tendency to relapse.

One patient was given 2,000,000 I.B.U. in four and a half weeks and showed rapid growth of a labial ulcer, the patho-

logical diagnosis of which is not yet obtained. One must, of course, consider the possibility of cancer stimulation by oestrin.

The two most severe cases were that of a woman who had an operative menopause seven years previously, and that of a woman of 63 who had had pruritus for ten years. These both necessitated very large doses before relief was established.

In all cases the local condition of the vulva was more normal both as regards appearance and secretion, which in some could only be described as succulent and juicy. Dyspareunia was ameliorated in a small number of these patients.

In one case a biopsy was made from the right side of the introitus and the typical condition of kraurosis was seen microscopically.

After treatment with 3,550,000 I.B.U. in seven weeks another biopsy was made on the opposite side of the introitus in a place as nearly symmetrical as possible to the former. The pathologist reported this to be practically normal tissue. The appearance of the whole section was more healthy, it was hyperaemic, and the round-cell infiltration had almost disappeared. Although the sections were not cut identically in the same plane, the squamous layer of the epidermis appeared thicker and more normal.

Macroscopically the vulva was similar in appearance except that the erosions of the surface were not seen, and the whole introitus was more succulent.

Clinically the patient was relieved of most of the irritation, which was less severe and less frequent. Treatment still continues with gradually decreasing doses, until full relief is obtained.

Conclusions.

(*a*) *Primary Amenorrhoea.* (One case). Practical benefit was not obtained.

(*b*) *Secondary Amenorrhoea.* (Twelve cases).

1. Menstrual bleeding can be guaranteed in 91 per cent of cases using the follicular hormone only.
2. Attendance of patient regularly is essential.
3. Cyclical application in the follicular phase is essential.
4. Continuation of cyclical bleeding after cessation of treatment occurs in a small number of cases.
5. Cyclical rhythm is re-started in some patients after a latent interval following cessation of treatment.
6. All symptoms of langour, tiredness, and loss of energy

disappear rapidly after three to five injections, with resultant improvement in general health.

(*c*) *Kraurosis Vulvae.*

1. Eight cases of kraurosis have been successfully treated.
2. Continued bi-weekly injections are necessary, with massive doses from the start.
3. Gradual reduction in dosage must be made.
4. There is marked improvement in the macroscopic appearance and of the secretion of the vulva.
5. Relief of dyspareunia.
6. Improvement in microscopic appearance with increased vascularity and diminution in small round-cell infiltration.
7. No change in colour of vulva until dosage is reduced.
8. Gradual relief from pruritus.
9. Better sleep.

I am greatly indebted to the Honorary Staff of the Gynaecological Departments for their co-operation.

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CASE HISTORIES.

CASE NO. 22. AGED 20. SINGLE. PRIMARY AMENORRHOEA.

Clinical observation. February 20th, 1935.

Menstrual history. She has never yet seen a period. Molimina started about three years ago, and she has had severe pain at monthly intervals.

Past history. Operation, bilateral herniotomy. No illnesses.

General. Secondary sex characters normal, and physically she is in very good health except for some langour. She has had treatment for some three years from various people without success. The last molimen occurred on February 5th, lasting two days, and was very severe.

CASE 22

PRIMARY AMENORRHOEA

1935		Days of ovarian cycle																											Dose of oestradiol benzoate
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
FEB.	16	50				10			10				10			10				10	[7	8]								100,000 I.B.U. or 10 mg.
MAR.	9	10				10			10				10			10														50,000 I.B.U. or 5 mg.
APRIL	6	10				10			10				10			10				10			10				50			120,000 I.B.U. or 12 mg.
MAY	4	50				50			50				50			50				50			50				50			400,000 I.B.U. or 40 mg.
JUNE	1	50				50			50				100			100				100			100				—			550,000 I.B.U. or 55 mg.
JULY	3	100		100				100			100					100			100				100					L	L	L	L	L	Nil	700,000 I.B.U. or 70 mg.
AUG.	14	100			—				100			100				100			—				100			100							600,000 I.B.U. or 60 mg.
SEPT.	14	100				100			100							—							150										450,000 I.B.U. or 45 mg.
OCT.	12	150							150							200							200										700,000 I.B.U. or 70 mg.

Patient could not attend any more.

Bold-face figures within brackets denote dates of menstrual bleeding.
Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.
L is Armour's corpus luteum injection = 3 gr. desiccated.

Treatment.

February 16th, 1935. After one dose of 50,000 and five doses of 10,000 I.B.U. and four dragees daily of 1,000 I.U., bleeding was seen for two days, but very very scanty. Second course: Injections of five doses of 10,000 I.B.U. were given, but with no more bleeding as a result. Third course: After the month was finished treatment was continued with bi-weekly doses of 10,000 I.B.U. for four weeks, when dosage was increased to 50,000 I.B.U. bi-weekly for six weeks. Again dosage was increased to bi-weekly 100,000 I.B.U. for nine weeks, and then there was a rest for five days. On the next five days 2 c.c. of Armour's corpus luteum, equivalent to three grains of desiccated gland, were injected.

August 14th, 1935. Still bleeding was not seen, and injections of 100,000 I.B.U. were continued bi-weekly. After nine injections the gynaecologist examined her under gas and apparently the cervix was normal and well developed. Possibly she had a unicornute uterus as there was palpable a mass extending out to the right with doubtful absence on the left. A sound entered one and a half inches from the nose of the cervix.

October 5th, 1935. As bleeding had not yet been seen and the patient could only come once a week, weekly injections of two doses of 150,000 and two doses of 200,000 I.B.U. were given.

October 26th, 1935. Patient has not attended after this date.

March 3rd, 1936. Patient reported that she had not yet bled.

Total dosage: 4,020,000 I.B.U. in eight months, and 1,400 dragées of 1,000 I.U.

Total cost, £32 15s.

CASE NO. 1. AGED 20. SINGLE. SECONDARY AMENORRHOEA FOR 10 MONTHS.

Clinical observation. October 4th, 1934. Periods absent for 10 months. Extreme langour and tiredness, complete lack of energy.

Menstrual history. Menstruation started at 13½ years, regularly every month lasting three days until 1933, when her father died, and from that time until now she has not seen any bleeding.

Treatment.

After seven doses of 50,000 I.B.U. bleeding started six days after the last injection and lasted four days. Second course: After two doses of 50,000 I.B.U. bleeding occurred for one day; cycle of 25 days. Third course: It was very difficult for the patient to attend regularly, and so four dragées only were taken daily for 14 days, but bleeding was not seen. Fourth course: Three doses of 50,000 I.B.U. restarted bleeding seven days after, lasting four days. Fifth course: Five doses of 50,000 I.B.U.. cycle 27 days, bleeding lasted three days, and epistaxis occurred on one day. Sixth course: Five doses of 10,000 I.B.U.; cycle 26 days. bleeding for one day only.

June 26th, 1935. Her general condition is very much improved, and she is free from langour and tiredness, but it is quite impossible for her to continue regularly to come for injections.

November 5th, 1935. Her occupation has been changed to that of a canvasser and she is out walking all day.

November 21st, 1935. Bleeding seen for two days; four diapers.

CASE 1.

Secondary Amenorrhoea—10 Months

1934	Days of ovarian cycle 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	Dose of oestradiol benzoate
Oct. 18	50					50				50			50			50			50				50						**[15**	**16**	**17**	**18]**				350,000 I.B.U. or 35 mg.
Nov. 19	—			50				—		50					—									**[13]**											100,000 I.B.U. or 10 mg.
Dec. 14																								Nil												
1935																																				
Jan. 14	50			50				50			—				**[31**	**1**	**2**	**3]**																		150,000 I.B.U. or 15 mg.
Feb. 4	50			50				50			50				50								**[27**	**28**	**1**	**2]**										250,000 I.B.U. or 25 mg.
Mar. 3		10			10				10			10				10									**[28]**											50,000 I.B.U. or 5 mg.
Mar. 29																								Nil												
April 29																								Nil												
May 7																								Nil												
June 4																								Nil												
July 2																								Nil												
July 30																								Nil												
Aug. 26																								Nil												
Sept. 23																								Nil												
Oct. 21																								**[14**	**15]**											
Nov. 16																										**[12**	**13**	**14]**								
Dec. 15																																		**[17**	**18]**	
1936																																				
Jan. 19																											**[14**	**15**	**16**	**17**	**18]**					
Feb. 19																					**[10]**								**[18**	**19**	**20**	**21**	**22]**			
Mar. 23																																				

Bold-face figures within brackets denote dates of menstrual bleeding.

Other figures refer to dose of oestradiol benzoate (in thousands of units) 1 at 50 = 50,000 I.B.U. given on any particular day of a cycle.

SECONDARY AMENORRHOEA

Case	Married or single	Age	Duration of amenorrhoea	Menstruation before amenorrhoea	General health	Treatment: Dose	Treatment: Duration	Treatment: Attendance	Results: General health	Results: Bleeding: During treatment	Results: Bleeding: Follow-up	Cost to May
1	S	20	10 months	Regular	Langour and loss of energy	1,010,000 I.B.U. or 101 mg.	35 weeks	Poor	Improved vitality and energy	Regular	No bleeding for 8 months, then started and has been regular for 5 months	£10 19 0
2	S	31	6 months	Irregular	Languor	480,000 I.B.U. or 48 mg.	9 weeks	Good	Great improvement	Regular	15 regular cycles	£5 12 0
13	M	32	17 months	Irregular	Obese	960,000 I.B.U. or 96 mg.	18 weeks	Failed to continue	No effect on weight	Regular	Failed to continue treatment	£9 16 6
24	M	33	18 months	Regular	Languor and tiredness	1,790,000 I.B.U. or 179 mg.	40 weeks	Missed several injections	Much improved. Misses the treatment now	Regular	No spontaneous bleedings	£19 16 4
25	M	22	9 months	Regular	Languor and loss of energy	1,750,000 I.B.U. or 175 mg.	38 weeks	Missed several injections	Very good. Plenty of energy	Regular	No spontaneous bleeding	£18 2 1
34	M	24	4 months	Irregular	Languor and sterility	1,240,000 I.B.U. or 124 mg.	21 weeks	Fair	Much improved. Still sterile.	Fairly regular	1 spontaneous bleeding to date after 3 months amenorrhoea	£10 19 8
39	S	20	20 months	Regular	Weight increased	2,100,000 I.B.U. or 210 mg.	27 weeks	Unable to attend regularly	No change in weight	Bleeding started. Four cycles	No difference	£13 14 6
48	M	23	24 months	Irregular	Obese	450,000 I.B.U. or 45 mg.	5 weeks	Failed to continue	No change in weight	Normal cycle produced	Failed to attend	£4 5 2
50	S	20	14 months	Regular	Fair	2,000,000 I.B.U. or 200 mg.	35 weeks	Irregular	Continuing treatment	Small cyclical bleedings	—	£17 3 0
55	S	18	15 months	Irregular	Severe molimina and languor	400,000 I.B.U. or 40 mg.	6 weeks	Irregular	Reduced pain. Improved health and vigour.	Regular periods	Still under treatment	£3 6 0
59	S	21	6 weeks	Irregular	Severe languor, tiredness and depression	500,000 I.B.U. or 50 mg.	9 weeks	Regular	Complete recovery. Return of energy	Regular periods	Just stopped treatment	£4 7 0
60	S	18	7 months	Regular	Loss of energy. Mental retardation	1,200,000 I.B.U. or 120 mg.	10 weeks	Regular	Increased vitality. No mental change	Nil yet after 1,200,000 I.B.U.	No success yet	£10 3 0

KRAUROSIS VULVAE

Case	Age	Married or single	Age at menopause	Symptoms		Treatment		Results					
				Degree	Duration	Dose	Duration	Relief	Time for relief	Relapse	Secretion	Endometrial bleeding	Cost to date
9	53	M	46	Severe pruritus	12 months	1,390,000 I.B.U. or 139 mg.	44 weeks	Good. Dyspareunia less. Coitus impossible before	6 weeks 450,000 I.B.U.	Two	Very good	One bleeding	£21 8 4
41	67	M	50	Burning soreness	6 months	360,000 I.B.U. or 36 mg.	3½ weeks	Local condition was improved. Pruritus not completely gone	Unable to attend			Nil	£2 19 4
43	50	M	44	Soreness	5 years	470,000 I.B.U. or 47 mg.	5 weeks	Fair. Not complete	Unable to attend for adequate time		Fair	Two bleedings	£6 8 0
54	52	M	45 operative	Very severe pruritus and fissures	14 months	5,520,000 I.B.U. continuing	21 weeks	Very good. Fissures healed. General health better	2½ weeks 1,100,000 I.B.U.	Nil	Good	Nil	£35 16 4
56	61	M	42	Vaginal atrophy, bleeding, and dryness	—	1,840,000 I.B.U. or 184 mg.	10 weeks	Improvement in general health and local condition	1 month	Nil	Excellent	One bleeding	£31 11 4
61	63	M	54	Very severe pruritus and ulceration	9 years	3,700,000 I.B.U. or 370 mg. continuing	7½ weeks	Fair relief of pruritus. Not complete yet. Sleep improved. Biopsies compared	7½ weeks 3,700,000 I.B.U.	Nil	Good		£22 6 0
62	45	M	35	Severe pruritus	7 months	2,000,000 I.B.U. or 200 mg.	4½ weeks	Fair. Rapid growth of large labial ulcer. ? chancre	Treatment stopped for investigation			Nil	£11 16 0
63	67	M	53	Severe pruritus. Insomnia	7 weeks	1,200,000 I.B.U. or 120 mg. continuing	2½ weeks	Great improvement in sleep. Irritation less severe and not so frequent	2½ weeks 1,200,000 I.B.U.	Nil	Good	Once	£7 11 0

December 15th, 1935. Bleeding for three days; cycle 29 days.
January 19th, 1936. Bleeding for two days; cycle 35 days.
February 10th, 1936. Bleeding for one day; cycle 23 days.

Result. (*a*) Her attendances were irregular and adequate treatment was unobtainable, and although bleeding was produced, no cyclical rhythm was possible. (*b*) As soon as her occupation was changed bleeding, although scanty, started spontaneously in cyclical rhythm, and she has improved considerably in health. Menstruation has been regular to date (March 22nd), and she has increased her weight by about 20 pounds.

Total dosage: 1,010,000 I.B.U. and 464 dragées of 1,000 international units.

Total cost, £10 19*s*.

CASE NO. 2. AGED 31. SINGLE. SECONDARY AMENORRHOEA (SIX MONTHS).

Clinical observation. Periods absent for six months, and languor.

Past history. Otitis media and otorrhoea for 12 years. Mastoid operation a month ago.

Menstrual history. Menstruation started at 14 years of age regularly every month lasting seven days; dysmenorrhoea before and on first and second days. Irregularity started three years ago, missed five months one year, next year missed five months. So far this year amenorrhoea for six months in June, when loss was very scanty for two days.

Treatment.

Three bi-weekly injections of doses of 50,000 I.B.U. produced bleeding immediately. Second course: Five injections of 50,000 I.B.U.; cycle 28 days, lasting six days. Third course: Four injections of 10,000 I.B.U., cycle 22 days, lasting five days; dysmenorrhoea first and second day. Fourth course: Four injections of 10,000 I.B.U.; cycle 28 days, lasting six days; six diapers; slight dysmenorrhoea. Following cessation of treatment she has had 15 normal periods of good loss averaging 22 to 29-day cycles.

Result. Very satisfactory as regards production of regular cyclical menstruation, continuing over a year to date after cessation of treatment.

Total dosage: 480,000 I.B.U. and 232 dragées.

Total cost, £5 12*s*.

CASE NO. 24. AGED 33. MARRIED. SECONDARY AMENORRHOEA (18 MONTHS).

Clinical observation. February 27th, 1935. Absence of menstruation since pregnancy 18 months ago.

Past history. Dilatation and curettage in 1924 for dysmenorrhoea and menorrhagia.

Menstrual history. Menstruation started at 13 years of age, lasting four to five days regularly every month. Dysmenorrhoea in hypogastrium first and second day. After her last baby was born in August 1933 she saw no more bleeding except for one day, when there was just a trace six months ago. She gets severe molimina each month, no climacteric disturbance, and she is languid and tired.

Treatment.

After treatment with five doses of 50,000 I.B.U. and four doses of 10,000

CASE 2

Secondary Amenorrhoea—6 Months

1934	Days of ovarian cycle	Dose of oestradiol benzoate
Dec. 13	50 50 [21 22 23 24]	150,000 I.B.U. or 15 mg.
Dec. 24	50 50 50 50 [15 16 17 18 19 20]	250,000 I.B.U. or 25 mg.
1935		
Jan. 21	— 10 10 10 10 [7 8 9 10 11]	40,000 I.B.U. or 4 mg.
Feb. 12	[6 7 8 9 10 11]	
Mar. 12	[29 30 31 1 2 3 4]	
April 5	[25 26 27 28 29]	
April 30	[18 19 20 21 22]	
May 23	[12 13 14 15 16]	
June 17	[7 8 9 10 11]	
July 12	[2 3 4 5]	
Aug. 6	[31 1 2 3]	
Sept. 4	[28 29 30 1 2]	
Oct. 3	[22 23 24 25 26 27 28]	
Oct. 29	[16 17 18 19 20]	
Nov. 21	[11 12 13 14]	
Dec. 15	[4 5 6]	
1936		
Jan. 7	[28 29 30 31 1]	
Feb. 2	[22 23 24 25 26 27 28]	
Feb. 29	[20 21 22 23]	
Mar. 24	[13 14 15 16 17 18 19]	
April 20	[7 8 9 10 11]	
May 12	[4 5 6 7 8]	
June 9		

Bold-face figures within brackets denote dates of menstrual bleeding.
Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.

Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.

CASE 24

Secondary Amenorroea—18 Months

1935	Days of ovarian cycle	Dose of oestradiol benzoate
	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35	
	——Leucorrhoea——	
Feb. 27	50 50 10 50 10 10 10 50 50	290,000 I.B.U. or 29 mg.
Mar. 30	50 50 50 50 50 [18 19 20]	250,000 I.B.U. or 25 mg.
April 21	— 10 50 50 50 [8 9 10 11 12 13 14]	160,000 I.B.U. or 16 mg.
May 15	50 50 50 50 50 [6 7 8 9 10 11]	250,000 I.B.U. or 25 mg.
June 12	50 50 50 50 50 [5 6 7 8 9 10 11 12 13]	250,000 I.B.U. or 25 mg.
July 14	Failed to attend [30]	
Aug. 10	50 50 50 50 50 [31 1 2 3 4 5 6 7]	250,000 I.B.U. or 25 mg.
Sept. 8	Failed to attend Nil	
Oct. 16	50 50 50 50 50 [6 7 8 9 10 11]	290,000 I.B.U. or 29 mg.
Nov. 12	10 10 10 10 10 50 [6 7 8 9 10 11]	90,000 I.B.U. or 9 mg.
Dec. 12	— — 10 — — Nil	10,000 I.B.U. or 1 mg.
1936		
Jan. 8	Nil	
Feb. 5	Nil	
Mar. 4	Nil	
April 1	[22]	
May 23		

Bold-face figures within brackets denote dates of menstrual bleeding.
Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.

I.B.U. she had a thick white vaginal discharge for seven days, and she said she had much more energy. Second course: Five doses of 50,000 I.B.U.; cycle 22 days, three-day loss, 10 diapers, less pain than every period before. She says she has been to doctors and institutions for two years without getting relief. Her family and friends have noticed a great improvement in her vitality. Third course: One dose of 10,000 and three doses of 50,000 I.B.U.; cycle 24 days, eight diapers, slight dysmenorrhoea. Fourth course: Five doses of 50,000 I.B.U.; cycle 28 days, six-day loss, slight backache, nine diapers. Fifth course: Five doses of 50,000 I.B.U.. cycle 32 days, nine-day loss, dysmenorrhoea absent, 10 diapers. Sixth course: Missed all treatment, cycle 17 days, one-day loss. Seventh course: Five doses of 50,000 I.B.U.; cycle 29 days, eight-day loss, nine diapers, dysmenorrhoea very slight. Eighth course: No treatment owing to holiday; not any bleeding. Ninth course: Five doses of 50,000 I.B.U.; cycle 27 days, six-day loss, eight diapers, slight dysmenorrhoea still. Tenth course: Four doses of 10,000 I.B.U. and one dose of 50,000 I.B.U.; cycle 30 days, six-day loss, eight diapers. Eleventh course: treatment was missed.

February 19th, 1936. Bleeding has not been seen since September when treatment was stopped. Patient was worried over her child who had scarlet fever, and attendance was irregular.

Total dosage: 1,790,000 I.B.U. and 868 dragées of 1,000 I.U.

Total cost, £19 16s. 4d.

CASE NO. 9. AGED 53. MARRIED. KRAUROSIS VULVAE.

Clinical observation. January 1st, 1935. Severe irritation of vulva for the last 12 months.

Menstrual history. Menstruation started at 13, regularly every 28 days, lasting seven days. In January 1934 it became irregular and ceased at 46 years. Twelve months ago severe vulval irritation and pruritus started which disturbs her sleep.

General. Flushes frequently but chiefly at night, headaches are frequent and bowels are costive. Micturition frequent, weight increasing.

On admission. General atrophic condition of vulval kraurosis.

Treatment.

January 1st, 1935. Consisted of bi-weekly injections of 50,000 I.B.U. and four dragées of 1,000 I.U. daily. No change was noticed until January 23rd, when flushes had disappeared and sleep was undisturbed, irritation being considerably less.

February 6th to February 13th, 1935. Pruritus very much easier, sleep good, no flushes. A white discharge was noticed after a total dosage of 400,000 I.B.U.

February 22nd, 1935. No flushes at all, irritation recurred, chiefly perianal. She gets a wonderful night's sleep now.

March 6th, 1935. Much sticky white discharge was followed by a streak of blood after 700,000 I.B.U. and no flushes at all. Irritation is now only felt occasionally.

March 16th, 1935. Coitus has been quite impossible since October 1934 owing to extreme pain. Patient asked if this can be attempted now. There is no increase in libido.

CASE 9

Kraurosis Vulvae

1935		Days of ovarian cycle: 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	Dose of oestradiol benzoate
Jan.	9	50			50				50			50				50										Nil										250,000 I.B.U. or 25 mg.
Feb.	6	50			50				50			50				50			50				50				50									400,000 I.B.U. or 40 mg.
Mar.	6	50			50				50			50				50					[**26**	**27**	**28**	**29**	**30**	**31**	**1**	**2**	**3**	**4**	**5**]					250,000 I.B.U. or 25 mg.
April	6																																			
May	1																																			
June	5	50			50				50			50				50																				250,000 I.B.U. or 25 mg.
July	3																																			
Aug.	1																																			
Aug.	29																				50															50,000 I.B.U. or 5 mg.
Sept.	26							50													50							50								150,000 I.B.U. or 15 mg.
Oct.	24							10							10						10							10								40,000 I.B.U. or 4 mg.
Nov.	21																																			

Bold-face figures within brackets denote dates of menstrual bleeding.
Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.

March 20th, 1935. Patient discharged by gynaecologist. Secretions were adequate and vulval condition was normal.

April 17th, 1935. Five days after patient was discharged bleeding started after being absent for seven years, and lasted 11 days with copious loss, six diapers daily. General condition excellent, no irritation, no flushes, and she has plenty of energy.

May 1st, 1935. No irritation, several small flushes again, no more bleeding. Sleep good. She was given four dragées of 1,000 I.U. daily again. Patient says coitus has been regularly weekly with complete comfort, but secretions are inadequate, resort being made to lubricant jelly.

June 5th, 1935. She has been completely free from irritation and flushes until now, when irritation has slightly recurred with a crack in the vulva again and poor secretion although coitus has been regular. Five doses of 50,000 I.B.U. were given bi-weekly after this, resulting in return to normal. She complained of slight tenderness in the left breast after the fifth injection. *Per oral* treatment was continued up to September 18th, when another crack occurred with slight irritation. Fortnightly injections of 50,000 units were then given until October 23rd, followed by weekly injectons of 10,000 I.B.U. up till November 20th when *per oral* treatment was continued for another 14 days.

February 27th, 1936. Her condition was quite permanent apart from very slight irritation and a still more occasional flush at night up to the present and was maintained by two dragées at night of 1,000 I.U. All treatment has now stopped.

Total dosage: 1,390,000 I.B.U. and 1,190 dragées of 1,000 I.U.

Total cost, £21 8*s*. 4*d*.

CASE NO. 54. AGE 52. MARRIED. KRAUROSIS VULVAE.

Clinical observation. Soreness of vulva.

Past history. Haemorrhoids early in married life. Seven years ago attended Mr. Smythe at the Homeopathic Hospital for excessive vaginal discharge and backache, left side. Diagnosed as pre-carcinomatous cervix, for which he performed panhysterectomy; both ovaries were healthy and left *in situ*. The pathologist reported "non-malignant cervical erosion." Fourteen months ago Mr. Shepherd performed perineorrhaphy as she was so badly torn with her last baby.

Obstetric history. Two children and one miscarriage.

Menstrual history. Menstruation started at 13 years, regularly every 28 days, lasting seven days; dysmenorrhoea on first two days. Menopause was operative. She had severe attacks of flushes following and still gets them. She is somewhat lethargic and irritable.

On admission. October 26th, 1935. Vulva, inside labia, was very sore and smooth and there were red patches here and there. In the region of the perineorrhaphy the epithelium was cracked and split, and bled readily on examination She was extremely sore, and complained of a very considerable and continuous irritation which interfered with her sleep. The introitus was narrowed.

Treatment.

She was given a local application of zinc oxide gr. 20, Ol. morrhuae

CASE 54

KRAUROSIS VULVAE

1935		Days of ovarian cycle 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Dose of oestradiol benzoate
OCT.	26	200				200			200				200			250				250			250			250				1.800,000 I.B.U. or 180 mg.
NOV.	23	250				250			250				250			200				200			200			200				1,800,000 I.B.U. or 180 mg.
DEC.	21	200				—			150				150			—				100			100			150				800,000 I.B.U. or 80 mg.
1936																														
JAN.	18	100				150			150				100			100				50			50			50				750,000 I.B.U. or 75 mg.
FEB.	15	50				50			50				50			—				50			20			20				290,000 I.B.U. or 29 mg.
MAR.	20	20				20			10				10						10						10					80,000 I.B.U. or 8 mg.
APRIL	17		10							10							10						—							30,000 I.B.U. or 3 mg.

Bold-face figures within brackets denote dates of menstrual bleeding.
Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.

CASE 61

KRAUROSIS VULVAE

1936		Days of ovarian cycle 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	Dose of oestradiol benzoate
JAN.	29	250			200				200		200			150		150		150			100		150		150			150		1,850,000 I.B.U. or 185 mg.
FEB.	26	200		200			200		250			250				250			250				250			200				2,050,000 I.B.U. or 205 mg.
MAR.	25	200			150				150			200				200			—				**[15**	**16**	**17**	**18]**				900,000 I.B.U. or 90 mg.
APRIL	19	—			150				150			150				—			150				150			150				900,000 I.B.U. or 90 mg.
MAY	16	150				150			150				150			150				100			100			100				1,000,000 I.B.U. or 105 mg.
JUNE	13	100				50			50				50			50				20			20			20				360,000 I.B.U. or 36 mg.
JULY	11	10				10			10																					

Bold-face figures within brackets denote dates of menstrual bleeding.
Other figures refer to dose of oestradiol benzoate (in thousands of units) given on any particular day of a cycle.

ad ℥i. Colour photographs were taken. Massive doses of dihydroxy oestrin benzoate were given bi-weekly and four dragees were taken per mouth before food daily.

November 2nd, 1935. She felt much improved and said she felt she could clean her house down from top to bottom. Slight relief of irritation yesterday and to-day. Photographs repeated closer up to patient in Dufaycolour and infra red.

November 2nd, 1935. Patient was much pleased and said: "The irritation is really very much better," and she had heaps more life.

November 13th, 1935. Markedly improved; no irritation at all, and she said "I am much more comfortable now than before my last operation 15 months ago."

November 16th, 1935. No irritation at all. Each morning she wakes up wondering if she will have any irritation, but she has had none.

November 20th, 1935. Severe stabbing pain in left breast. Mr. Shepherd examined her and was very pleased indeed, and made a vaginal examination without causing pain, but she was sore afterwards owing to some spitting again.

December 4th, 1935. No irritation at all. Dragées increased to seven daily, equal to 7,000 I.U. daily.

December 7th, 1935. No irritation at all. Urine taken from early morning on December 8th for Zondek-Aschheim test for photographing uterine reaction on mice.

December 12th, 1935. A further series of photographs was taken in Dufaycolor and infra red. Patient was very happy and comfortable, but there were still some colour changes of the vulva in the vestibule but these were not quite so bright. No fissuring.

Result. (*a*) Rapid reaction to progynon. (*b*) Relief of irritation. (*c*) Improvement in well-being and health. (*d*) Slight improvement in colour change. (*e*) Improvement in vascularity and epithelization of the vestibule.

Observations. On reducing dosage it was found that one injection weekly was not sufficient to keep her free from irritation. Two injections of 100,000 I.B.U. weekly were then given, but irritation still recurred, and 150,000 I.B.U. twice weekly was then found to be the minimum bi-weekly dose necessary at the time. Gradually the dose was reduced and is being maintained for some while until symptoms fail to recur. Both the general and local condition of the patient have markedly improved.

Total dosage: 5,500,000 I.B.U. and 600 dragées of 1,000 I.U.

Total cost, £35 16*s.* 4*d.*

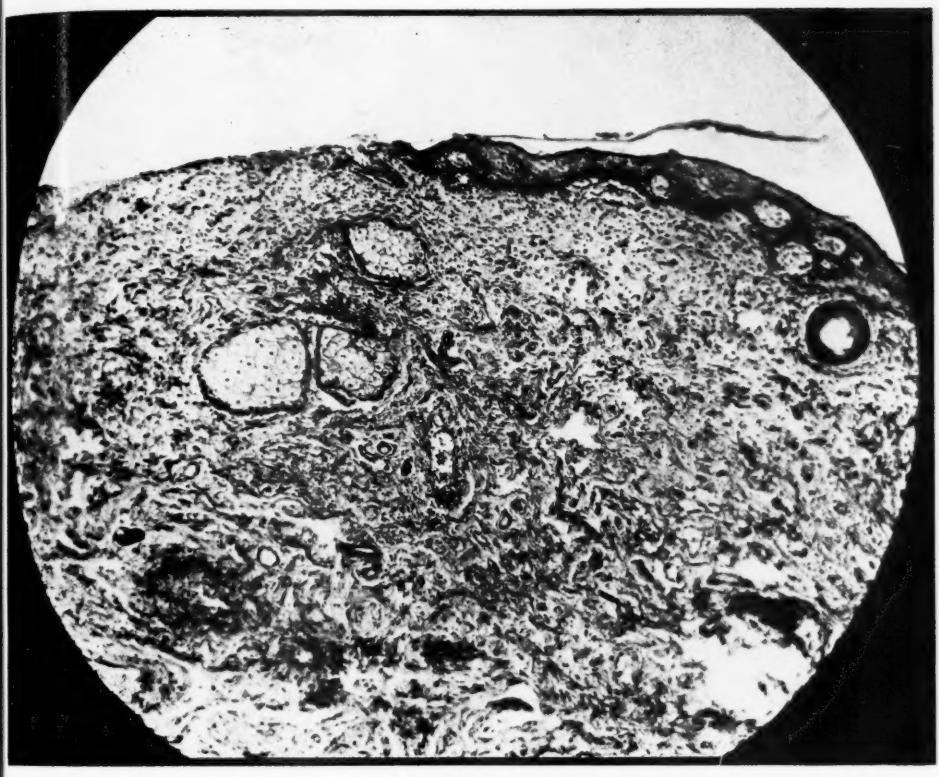
Case No. 61. Aged 63. Married. Kraurosis Vulvae.

Clinical observation. Severe irritation of vulva for the last 10 years.

Menstrual history. Menstruation started at 15 regularly every 28 days, lasting from five to seven days. Menopause at 54, slowly and gradually. She gets occasional flushes but they do not bother her. Constipation slight. No headaches. Sleep very poor owing to smarting and irritation, which is very severe at night—"like a burnt finger."

On admission. Gynaecological reports: "Senile atrophic labia and vulva with some carunculosis and erythematous discoloration of vestibule."

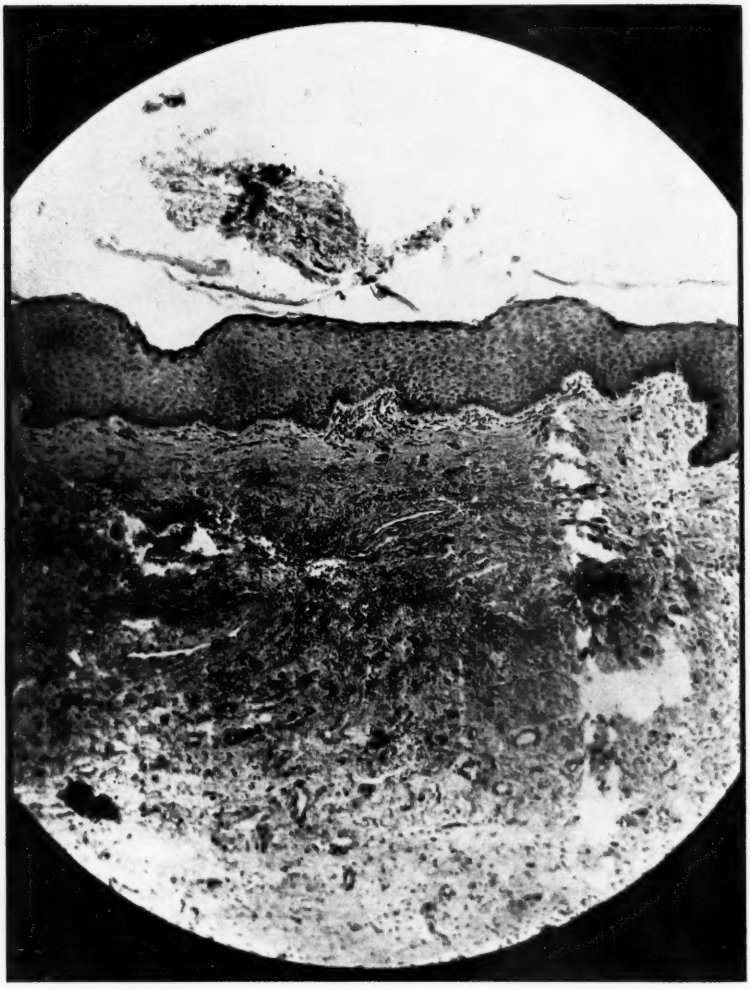
January 29th, 1936. Small portion of skin of right labium minus removed



Microphotograph of Section of Biopsy Taken Before Treatment Started on 29th January, 1936.

The biopsy was made from the right side of the vestibule.

The Pathologist reported: "The dermal layer is fibrosed and infiltrated in places by plasma and round-cells. The epidermis shows hyperkeratinization, and in places is atrophic and even ulcerated. There is no evidence of any malignant change. The picture is that of kraurosis vulvae."



Second Microphotograph After Treatment with 3,550,000 I.B.U. in Seven Weeks. (18th March, 1936.)

Biopsy was taken from the opposite side of the introitus in a place as nearly symmetrical as possible to the former.

The Pathologist reported: "Except for some slightly increased vascularity of the dermal tissues, and a very occasional small area of round-cell infiltration, the tissue is normal in appearance. There is nothing abnormal in the appearance of the epidermis."

for section. Pathologist reported: "The dermal layer is fibrosed and infiltrated in places by plasma and round cells. The epidermis shows hyperkeratinization and in places is atrophic and even ulcerated. The picture is that of krausosis vulvae."

Treatment.

At first bi-weekly injections of 250,000 and 200,000 I.B.U. were given with five dragees daily of 1,000 I.U. before food.

February 2nd, 1936. Considerable irritation still from stitch area.

February 10th, 1936. Injections now given three times a week. Irritation eases off after injections but tends to recur afterwards. The vulva after 1,000,000 I.B.U. was extremely succulent and less reddened although she still complained of slight irritation.

February 19th, 1936. It seems necessary to give three injections weekly of 150,000 I.B.U.

February 26th, 1936. Irritation still persists two days after injections, so dosage increased to three injections weekly of 200,000 I.B.U. Gynaecologist was very pleased with local condition, which appears practically normal except for atrophy.

March 2nd, 1936. Irritation slightly easier, completely absent yesterday, but recurred during the night. Injections twice weekly of 250,000 I.B.U.

March 18th, 1936. A second biopsy was taken from the opposite side of the introitus in a place as nearly symmetrical as possible to the former after the patient had received a total dosage of 3,550,000 I.B.U. in seven weeks. The pathologist reported that "except for some slightly increased vascularity of the dermal tissues and a very occasional small area of round-cell infiltration the tissue is normal in appearance. There is nothing abnormal in the appearance of the epidermis."

March 30th, 1936. The dosage is being gradually reduced now since the skin condition is shown to be normal. The irritation is infrequent and not so severe, and the local condition is very good.

Total dose in seven and a half weeks, 3,700,000 I.B.U.

Total cost to March 19th, 1936, £22 6*s*.

Red Light Treatment in Gynaecology.

BY

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Assistant in the Physical-Therapeutic Department of the Gynaecological Clinic of Amsterdam University (Prof. v. Rooy).

FOR a long time physical therapy has been applied in gynaecology, and yet many a subdivision of this therapy is still regarded by some with little faith and is ignored by others. This also applies to light therapy. Yet there are reasons for such an unfavourable standpoint, and these are chiefly due to the lack of a thorough scientific base. Physical therapy belongs for the greater part to experimental medicine. Except for a few proved facts, as for instance the influence of ultra-violet light rays on rickets, we are still in the experimental stage so far as light therapy is concerned. The most studied section is that of ultra-violet light rays; all the same, the conviction is growing more and more that the visible light can also exercise a considerable influence on the human organism. Visible light is composed of seven colours: red, orange, yellow, green, blue, indigo, and violet. Light is an ether vibration, the same as electricity and Röntgen and radium rays. All these ether vibrations have a velocity of 300,000 km. per second, but the number of vibrations per second is different for all ether waves; this frequency can be calculated. Red light has a vibration frequency of 370,000,000,000,000. In any case we are accustomed to denote the rays, not according to their vibration frequency, but according to their wave-length. Working by the formula: Motion velocity = wave-length × vibration frequency, we find for red light a wave-length of 0.000081 cm. = 0.810 micron = 810 millimicron.

The other extreme of visible light, violet, has a wave-length of 390 mm. We can graph the various kinds of rays by arranging them according to the size of their wave-lengths; this is called the electro-magnetic spectrum (Fig. 1). The longest are the electrical waves, especially the waves of wireless telegraphy and telephony (up to 10,000 metres). The shortest are the Röntgen and radium waves (up to 0.01 mm). Above the visible light we find the ultra-red and on the other side the ultra-violet.

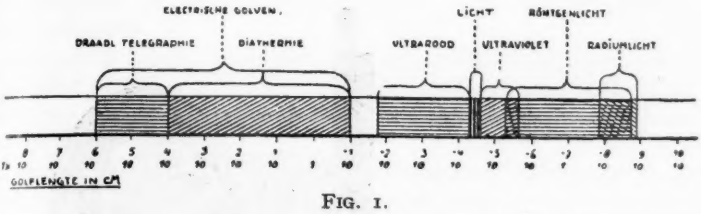

FIG. 1.

Immediately past the infra-red light are the diathermic waves. The visible light, therefore, takes only a very small place in the electro-magnetic spectrum. Thus one can construct a light source which radiates exclusively red rays, but the activity is dependent on the intensity as well as on the wave-length. We make use of two different light sources in our red-light therapy. One is the so-called lamp of Küstner (Fig. 2), which is composed of a

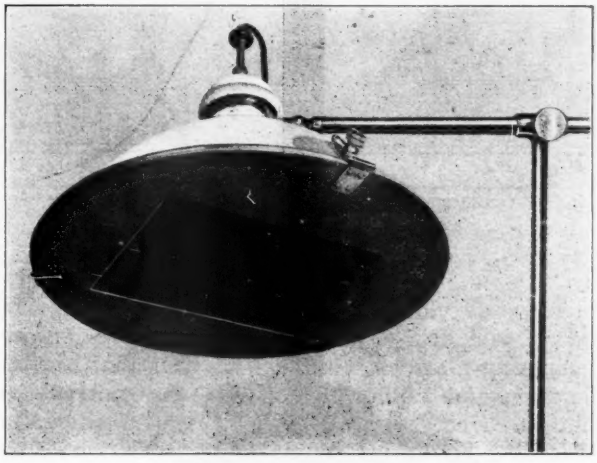

FIG. 2.

glowing metal filament lamp of 40 watts, which is enclosed in a reflector to which a red glass is attached. (Through this particular red glass only rays of 700–800 mm. can pass.) The other source of greater intensity is the neon lamp (Fig. 3), composed of spirally wound glass tube filled with neon gas, which radiates red-orange light. We know that the ultra-violet rays are absorbed directly at the surface; they do not penetrate for more than $\frac{1}{2}$ mm. into the skin. Visible light penetrates far more deeply into the

FIG. 3.

skin and also under the skin. Red light especially has a great penetrating power, as can be seen in the following graph (Fig. 4).

A few biological effects of light have been well studied, such as the formation of pigment of the skin, the bactericidal effect,

the influence on blood and metabolism, and the influence on blood-pressure.

We shall here occupy ourselves only with what is known of the effect of red rays on the animal organisms, i.e. of the rays between about 700–800 mm. The treatment with red light has been applied since the middle of the last century, but was discontinued because the results were negative. Changes were not observed on the skin, although changes were observed on the skin when ultra-violet and infra-red rays, equal heat rays, were applied. It was assumed, therefore, that these red rays could not have any biological effect. At present it is known that the

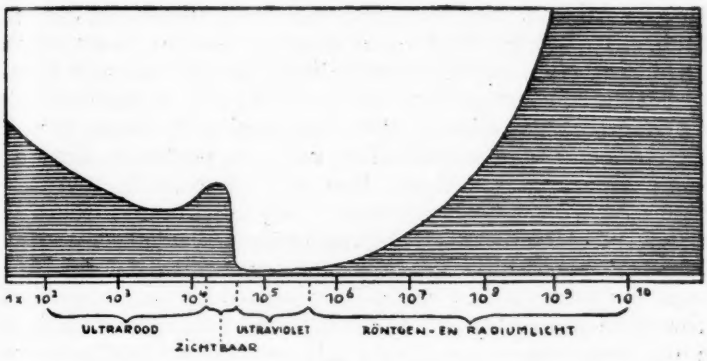

FIG. 4.

red light passes through the skin and is only absorbed in the deeper layers. It appears that the red rays are largely checked by the muscle and fascia, so that these act as a protection. Can red rays, therefore, act therapeutically on the human organism? Various investigations indicate that red rays have an influence on the hormones. Küstner, especially, has occupied himself with this problem in the obstetrical clinic of the University of Leipzig. His observations have proved to be valuable for gynaecological therapy. In view of Küstner's work Professor van Rooy was induced to make the necessary provisions in the physical therapeutic section of the obstetrical clinic at Amsterdam, so that investigations could be carried out and therapy with red light could be applied. What has been ascertained by various tests with animals? Küstner and also Ludwig and von Ries alternately treated the follicle hormone, progynon, with red and ultra-violet light respectively. After treatment this hormone was

injected into a white mouse to study the biological reaction. It was seen, when the hormone had been treated with ultra-violet light, that it had lost its activity, while its activity was greatly increased after treatment with red light. The progynon made ineffective by ultra-violet light could be activated again by red light. Red light, therefore, activates this hormone, while its action is checked by ultra-violet light. This is exactly the opposite of what can be observed in the case of ergosterine. This is activated by ultra-violet and made inactive by red light. We do not know what exactly happens to progynon after light treatment, as the chemistry of this hormone is unknown to us. What effect has red light on the other hormones? Küstner and Eissner together have investigated the effect of red light and ultra-violet light on insulin. They determined the blood-sugar quantity in the rabbit after it had been injected with ordinary insulin and with light-treated hormone, but no difference was observed. A positive result has not been obtained with either thyroid gland hormone or with the hormone of the posterior lobe of the hypophysis. Tests on animals by Ludwig and von Ries show that red light has an influence on the growth hormone. They bred rats subjected to the rays of red light, blue light, and ordinary daylight. All these animals lived under the same conditions and were fed in the same way. The animals kept in red light showed by far the quickest growth; they were heavier by 80 grams than the rats which lived in blue and ordinary light. Thus it is seen that red light increases growth.

The following test by Küstner shows that red light has an influence on the sex hormone. It has a stimulating activity. He proved that the reaction of Aschheim and Zondek was made more rapid when this test with rats subjected to red light was carried out. In this test he used four small wooden boxes, provided with glass on one side. The first box contained blue glass which let through ultra-violet light, the second green, the third orange, and the fourth red glass, so that the test animals were kept in four different colours of light, this being started two days before injections of the urine were made. As light source he used a 60-watt glowing-filament lamp, which was placed 5 cm. from the glass; he did not use daylight, for this is unreliable, especially as concerns the ultra-red and ultra-violet rays, which are present to a far smaller extent when the weather is overcast. As has been described, the mice were placed in the different boxes a few days before the injections; they were then injected in a weak artificial light and directly afterwards returned to the boxes.

The swiftest reaction was registered with red and orange light. After about 55 hours definite indications of pregnancy were discerned. In the positive reaction definite follicle enlargement, haemorrhage, and a considerable enlargement of the uterus was noticed, while the animals kept in blue and green light did not show, practically, any reaction. After 72 hours the difference was still more noticeable. The mice kept in red and orange light showed a very marked formation of corpora lutea, while with the others only enlarged follicles and haemorrhage were noticed. The red light not only speeded up and strengthened the reaction of the Aschheim-Zondek test, but the mice had also more power of resistance and, therefore, the reaction of Aschheim and Zondek is nowadays always performed in red light at Sellheim's clinic. Further, it has been proved with the male animal that the spermatogenesis is strengthened when the testicles are treated with red light.

From these tests one may, therefore, conclude that light has an influence on the sex- and growth-hormone, in the sense that red light has a stimulating and ultra-violet light a retarding action.

How and when can we apply red light to our gynaecological patients? It is clear that those abnormalities must be treated which are caused by a shortage of sex hormones, or by an insufficient reaction of these hormones. In the first place we think of hypoplasia of the sex organs. Landeker treated patients with hypoplasia and aplasia with ultra-violet light applied in the vagina and at the same time with red light applied externally; the treatment was accompanied with organic extracts or without them. He obtained favourable results, which he ascribed to the results of hyperaemia and to an improved constitution.

Nowadays it is accepted that the effect is due to an influence on the hormones. In France good results were obtained with the treatment of melancholic patients with red light; we know that psychic disturbances in the case of women are often accompanied by under-function of the sex organs and, therefore, this favourable action can be well understood. According to Küstner menorrhagia in puberty, i.e. the juvenile haemorrhages, and also very violent dysmenorrhoea, more especially membranous dysmenorrhoea, are caused by under-function of the sex-hormones. In these abnormalities he obtained very favourable results with the red-light treatment. The patients, however, must be treated often and for long periods, at the beginning an hour a day, after 15 light treatments once or twice a week. In the case of

sterile women in whom an internal genital organ abnormality cannot be palpated, Küstner applied the red-light therapy twice successfully, although previously local gynaecological treatment with organic extracts and medicinal baths had no effect. With male sterility also, due to oligospermy, it appears that the treatment of the testicles gives a favourable result.

In the first place we have tested the treatment with red light in four cases of juvenile haemorrhages; in each case a good result was registered. The first case concerned a girl, 17 years of age, who continually had menorrhagia; once it was so serious that her uterus had to be curetted. Pathologic anatomically normal mucous membrane was found. Red light was then applied (25 times by the lamp of Küstner) and after that she twice menstruated normally for a period of four days.

The second case concerns a girl of 17 years of age, who menstruated irregularly, mostly far too often and always too profusely. She also had dysmenorrhoea. Further, she was melancholic, and for this she was treated at the neurological policlinic. Red light was then applied (neon lamp, 12 times). After an interval of 26 days she menstruated from 4th to 10th December, not profusely, although painfully. From 5th to 10th January she had a normal menstruation again. Subjectively, the result was remarkable. The girl was brighter and more cheerful, and for the time being further visits to the neurological policlinic were unnecessary.

The third patient is a girl of 19 years of age, who for the last few months had been suffering from abnormal menstruation. The interval was one to two weeks, and menstruation was very painful; after treatment with red light menstruation became normal; the pain, however, persisted.

The fourth girl is 16 years of age, and was menstruating profusely every fortnight. After 10 treatments with red light menstruation ceased for $3\frac{1}{2}$ weeks and lasted merely four days. We thus obtained the impression that red light has a favourable effect on juvenile haemorrhages. Subsequently we treated four patients of about 30 years of age, all married and childless. By palpations, abdominal and vaginal examination, the genital organs appeared to be normal. The patients complained respectively of menorrhagia and metrorrhagia with or without pain. After red-light treatment the interval between menstruations was longer and the period of menstruation shorter in three out of four patients, but the menstrual pain did not disappear. Their general state of health improved. Also in these patients a

retarding influence of red light on uterine haemorrhage was seen. The patients were treated 8–30 times. The distance of the light source from the patient was always 40–50 cm.

In the case of four girls, who complain only of dysmenorrhoea, we have not had any success up to the present. In the case of a married woman of 33 years of age, with slight hypoplasia and violent menstrual pain, we obtained a favourable result after 20 treatments. The pain from which she had suffered for five years did not reappear. Finally we treated three other patients for amenorrhoea. In addition to red light, menoninform injections were used. The diagnoses were respectively: infantilismus ($1\frac{1}{2}$ years' amenorrhoea), atrophy of the uterus (four years' amenorrhoea), and climacterium praecox (two years' amenorrhoea). In none of these patients was there any subsequent menstruation. The patients, however, felt better after the treatment.

All these patients have been radiated with the lamp according to Fig. 2 and Fig. 3, viz. with the lamp of Küstner (Fig. 2) on the abdomen and with the neon lamp (Fig. 3). [Manufacturer: Franken Pohl, Rohin 100, Amsterdam] on the whole front-surface of the body. The distance of the source of light was 40–50 cm., and the duration of the treatment 30 to 45 minutes. Also a lamp has been designed for vaginal application (Fig. 5). [Manufacturer: E. C. A., Amsteldijk 205, Amsterdam.] This is a curved neon tube, surrounded by a glass mantle, which mantle has a diameter of 3–4 cm. This apparatus is inserted into the vagina, and the duration of radiation is 30 to 45 minutes. We used this apparatus for the treatment of pruritus vulvae et vaginae, alternately changed with the lamp for general radiation. Very often we obtained a surprisingly good result.

A very good example is the following case. A patient, 30 years of age, who suffered from pruritus vulvae et vaginae, had such an excruciating itching that, after injections with novocain did not give any results, the operation of Cotte (the cutting of the presacral nerves) was performed. A month later the itching came back. Six months after this she was treated with Röntgen rays, which also did not procure any success. At last we tried to cure her by means of red-light radiation. The neon tube was applied vaginally. After 15 treatments the itching had entirely disappeared and up to now has not returned. The last treatment with red light took place one year ago.

We also had favourable results in the treatment of kraurosis vulvae and eczema vulvae, on which occasions we mostly com-

bined the vaginal treatment to the external radiation of the vulva. Thereupon we applied the vaginal treatment in some cases of adnexitis, which had not reacted favourably to diathermy and hot irrigation, the top of the neon tube being placed against the tumour. Since red light can achieve hyperaemesis in the lower tissues, the favourable therapeutical result thus obtained can probably be attributed to this fact.

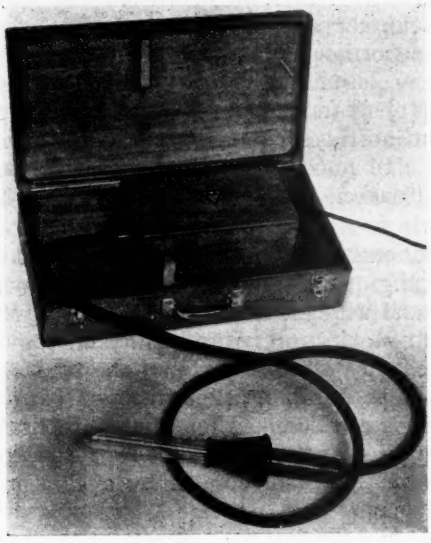

FIG. 5.

Up to now regularly we used for menorrhagia the lamp for external radiation, but have now begun to try the vaginal application, especially in the case of patients with cyst degeneration of the ovaries. (It is evident that we do not apply the vaginal tube to a virgin.) The neon tube is used only during the intervals of bleeding. Whether the vaginal treatment of menorrhagia will give a better result than general radiation cannot yet be judged.

From our observations we can, therefore, conclude that red light has a retarding effect on abnormal uterine haemorrhage especially on haemorrhages in young women.

It is noteworthy that the general health condition of the patient improves greatly, probably as the result of a change in the composition of the hormones. In the case of dysmenorrhoea and sterility we have not yet been able to determine any definite result

SUMMARY

A discussion concerning some experiments on small animals demonstrates that red light has a stimulating influence on the hormones of growth and sex. Clinical success has been attained with red light in patients suffering from metrorrhagia and menorrhagia, especially at puberty. Sometimes red light has a good result with pruritus vulvae and adnexitis.

RÉSUMÉ

L'auteur discute quelques expériences sur des animaux pour montrer que les hormones sexuelles et les hormones de croissance peuvent être activées par des rayons rouges. En thérapeutique humaine, de bons résultats on été obtenus chez des malades avec hypofonction des organes génitaux, c'est à dire chez les ménorrhagies et les métrorrhagies, surtout chez les ménorrhagies de la vierge.

A Study of Variations in the Number of Blood-platelets during the Menstrual Cycle.*

BY

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THE rhythmical changes which characterize woman's menstrual or sexual cycle are not confined to the genital organs. Parallel with the changes in the ovaries, Fallopian tubes, uterus and vagina, changes that are now tolerably well known both in a histological respect and in regard to their hormonic regulation, certain general changes of a psychical as well as physical nature have for long been observed. These have been considered in relation with the different phases of the menstrual cycle, attention having been principally directed to changes occurring in immediate connexion with the menstrual period itself. To a large extent, however, the views on these changes are built upon general impressions and disconnected observations, and not until recent times have individual organs and organic functions been subjected to systematic investigation, with a view to arriving at a more exact demonstration of these rhythmic changes, and their relation to different phases of the monthly cycle. As from about the same time a substantially deeper insight into the hormonic regulation of the menstrual cycle has been gained, attempts have also been made to put the demonstrated changes into causal relation with those hormonic displacements that have been shown to be the direct cause of the changes in the genital organs themselves.

The fact that among other changes, menstruation involves bleeding from the blood-vessels injured at the shedding of the uterine mucosa has directed interest more especially to the blood changes which attend the phases of the menstrual cycle. Attempts have been made to demonstrate (1) numerical changes in the corpuscular elements of the blood, and (2) changes in the blood-

* This investigation has been conducted with assistance from the fund instituted under the name of "Stiftelsen Thérèse och Johan Anderssons Minne," Karolinska Institutet, Stockholm.

sedimentation reaction as well as the coagulation time of the blood.

Evidence has been found of a premenstrual increase of the red corpuscles, which is absent in anaemic women, an erythropenia during the actual period of menstruation, and a postmenstrual increase in the erythrocytes. A menstrual and postmenstrual leucocytosis is likewise considered to have been demonstrated with certainty. (Jagic and Hickl[1]).

The blood-sedimentation test shows a distinct increase during menstruation (Hubert[2]). The clotting time of the blood is prolonged at menstruation (Jagic and Hickl), and the stasis test (Rumpel-Leede's test) is positive (Henning[3]).

The third of the formed elements of the blood, the platelets, did not receive attention in this connexion until lately. Pfeiffer and Hoff[4] were the first to show that the platelet-content of the blood falls at menstruation to one-half or less of its normal value, the lowest value being reached on the second day of menstruation, after which the level rises slowly to normal. These observations have since been tested and verified by several investigators (Henning, Francesco,[5] Sakai,[6] Benhamou[7] and Nouchy, Kato,[8] *et al.*), but are called in question by others (Hirsch and Hartmann,[9] Denisova-Suscevskaja[10]).

The reduction which occurs in the platelets at menstruation and the simultaneous lowering of the capillary resistance have given rise (Henning) to rather far-reaching theories to the effect that menstruation is to be regarded as a physiological thrombopenia with a general liability to bleeding, or as a downright latent haemorrhagic diathesis, and that these changes are dependent on the female genitalia. This notion has in fact led to experimental studies with a view to correlating the blood-platelet value and the female sex hormones.

It was this latter notion which induced the author to institute a fresh investigation in the hope that he might thereby reach a comparatively simple method of determining fluctuations in the hormone titre. It was more especially in respect of oestrin, the concentration of which in the organism changes as is known in a typical and regular manner in connexion with the different phases of the monthly cycle (Siebke, quoted from Genell[10]). However, it very soon became evident that this object was not attainable, and that the investigation, therefore, did not offer any prospects from this point of view.

A study of the literature showed that none the less the investigation need not be fruitless, and this for the following reasons:

There is not any concord of opinion as to whether the platelet value actually falls at menstruation, and none at all as to the degree of any such fall. All the investigations I have come across are based on such small materials that the mean values cannot but be greatly influenced by individual variations, and the errors inherent in all methods of blood-platelet count. The degrees of the changes in the number of platelets during menstruation cannot, therefore, be considered as established. As this has a certain bearing on the view of the physiological significance of these changes, there was here a further reason for carrying out the contemplated investigation.

I. *Does the number of blood-platelets vary in a typical manner during the menstrual cycle?*

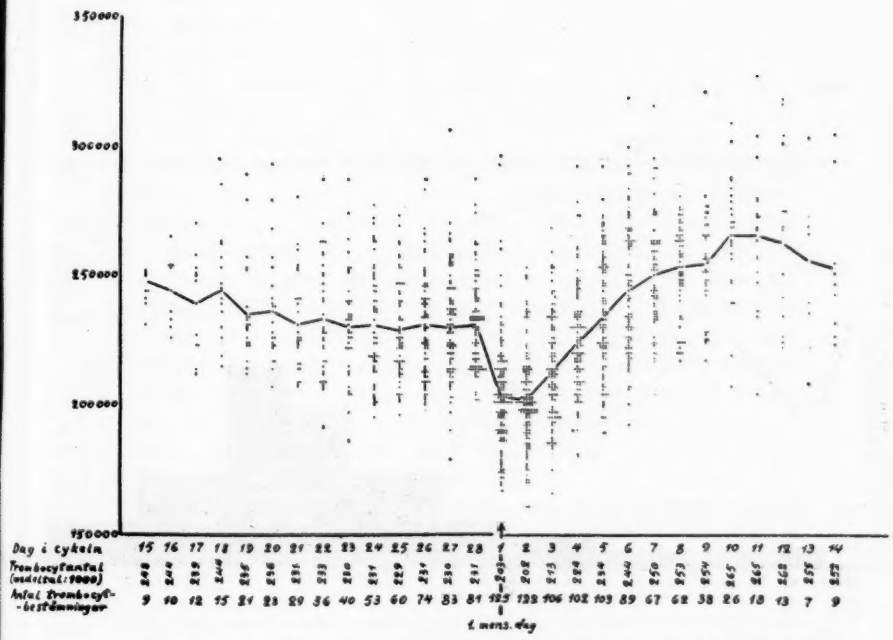
My investigation comprises 1,433 platelet counts on 38 normal women ranging from 18 to 30 years of age (probationary nurses and midwives who had voluntarily offered their services as subjects). All had a normal monthly cycle of about 28 days duration and normal periods of four to five days duration. The method of platelet count used by me is the one worked out by Kristenson.[11] The samples of blood were drawn at the fingertip (Norman[12]), so far as possible at the same time of the day for the same person to avoid possible variations due to meals. So far as possible samples were taken from each test-subject daily over at least one menstrual cycle, usually over two or more.

The result of the test is graphically indicated in Fig. 1. Each dot represents a platelet determination. The variations, which naturally include both variations due to errors attaching to the method and individual variations, can be seen direct from the curve. So long as the number of determinations per day is 30 or more, the curve drawn through the mean values has a smooth course. The irregularities in the curve for a lower number of determinations seem to me to indicate that the lower number in question is not sufficiently high to level out the influence of individual variations and test errors. This should cast some light on the value of previous investigations, since earlier investigators never obtained their mean values on the basis of more than 10 determinations, often of only two or three.

The results of the investigations, so far as they can be elicited from the curve (Fig. 1), are as follows:

1. The normal number of blood-platelets during the week preceding the menstrual period is 230,000 per c.mm.

2. On the first day of menstruation the number of platelets is



Trombocytantalets variationer under menstruationscykeln.

1433 bestämningar på 38 normala kvinnor mellan 18 och 30 år.

Fig. 1

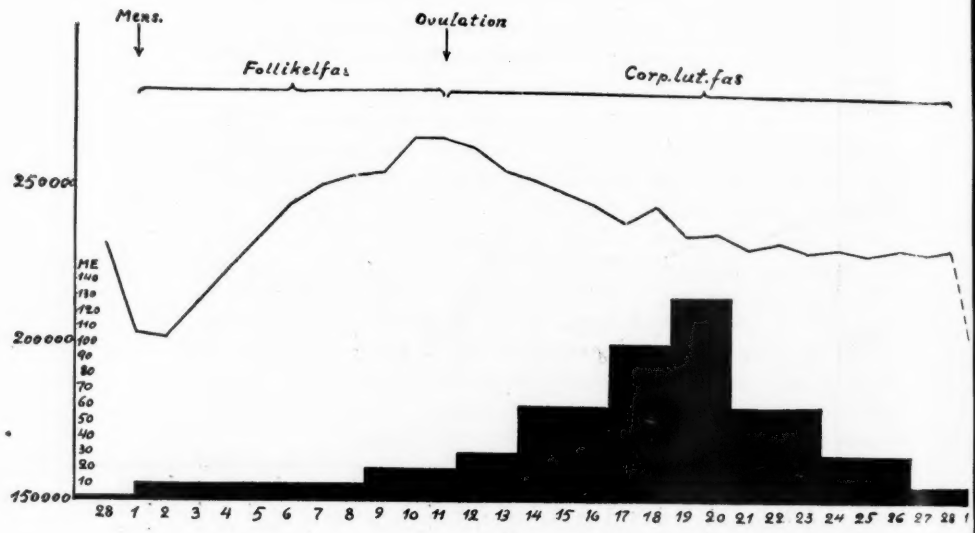

Mens.
Ovulation
Follikelfas
Corp.lut.fas
25000
200000
150000
ME
140
130
120
110
100
90
80
70
60
50
40
30
20
10
28 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 1

Fig. 2

suddenly reduced to about 200,000, i.e. by about 13 per cent. The lowest value is reached on the second day of menstruation.

3. From and including the third day and during the week immediately following menstruation there is a slow and regular rise in the number of platelets, the highest point being reached on the tenth or eleventh day of the menstrual cycle, when the value is about 265,000.

4. During the period from the twelfth to about the twenty-first day of the monthly cycle the number of platelets slowly sinks to about 230,000, at which value it persists until the onset of menstruation.

In agreement with most earlier investigators I have accordingly found an abrupt fall in the number of blood-patelets, a "Thrombocytensturz," to occur at menstruation, but this fall is not so great as most workers have been inclined to assert. It amounts only to 13 per cent of the normal value, whereas Pfeiffer and Hoff, Henning, Kato and others give one half to four-fifths of the normal value. This expression of a thrombopenia, a latent haemorrhagic diathesis, which some of these authors have wished to see in the extremely low platelet value at menstruation must, therefore, in my opinion, be considered as dubious. Isolated individuals doubtless exhibit such low platelet values at menstruation, and no doubt a count here and there may fall so low, but my curve shows that these findings are due to pure chance factors. If the mean values are derived from such few counts as those made by the authors mentioned, the curve may happen to show fluctuations of this extreme nature. A sample of sufficient size to exclude the influence of these variations will give a result which shows that really thrombopenic values do not occur at menstruation, for with a platelet count of 200,000 per c.mm. there is no thrombopenia.

This reasoning is obviously not prejudiced by the fact that the earlier investigators used a different method of platelet count (Fonio), which constantly gives somewhat higher values.

The question put at the head of this section can, therefore, be answered to the effect that the number of blood-platelets varies in a typical manner during the menstrual cycle.

II. *Do these variations stand in causal relation with the physiological phenomena in the genital organs during different cyclical phases?*

The amount of the menstrual flow is estimated at 30 to 50 c.c. (Fraenkel[13]). Pfeiffer and Hoff have bled men of the same quantity of blood without being able to find any resulting

diminution in the number of blood-platelets, still less any abrupt fall. Benhamou and Nouchy have shown that the fall of the platelet level begins before the external flow itself commences, even so long before as about 12 hours. It, therefore, appears that we can conclude that the blood-platelet fall at menstruation is not related to the actual menstrual flow as such.

Among earlier authors, Pfeiffer and Hoff and particularly Henning as well as Denisova-Suscevskaja[14] assumed a connexion between the blood-platelet changes and the variations in sex hormones that take place at menstruation. In Fig. 2 the blood-platelet curve has been correlated with the hormonic phases during the menstrual cycle. The concentration of hormones in the organism during these phases is admittedly imperfectly known, but so much we know with certainty, that the corpus luteum hormone, progesterone (*Klin. W. Schr.*, 1935, p. 1182), is secreted only during the period after ovulation and that its concentration sinks just before menstruation, when the corpus luteum exhibits signs of degeneration. It may doubtless be considered as established that the functional change of tone in the myometrium at menstruation (increased sensitiveness to the posterior lobe hormone) depends at least to some extent on the cessation of influence from the corpus luteum hormone. As the change in the tone of the myometrium takes place within 24 hours, the concentration of corpus luteum hormone probably declines at a corresponding rate. The concentration of oestrin is better known. It rises in both blood and urine during the first three weeks of the cycle, the highest concentration being reached about the 19th to 20th day. On Fig. 2 I have traced the curve showing the urinary elimination of oestrin established by Siebke and shown by him to be roughly parallel to the hormone curve of the blood. From a glance at Fig. 2 it appears possible to put the sudden diminution in blood-platelets at the onset of menstruation into causal relation with the extinction of the corpus luteum hormone. And possibly some parallelism may be said to exist between the oestrin curve and the platelet curve during the intermenstrual period.

Bankow[15] has submitted the question to an experimental study. He adopted Kristenson's method of blood-platelet count on white rats. The test animals were divided into three groups: (*a*) animals operatively castrated by oöphorectomy or orchidectomy; (*b*) animals castrated by ligation of the vessels to the sex-glands; (*c*) animals hyperhormonized by subcutaneous administration of fresh homologous sex-gland in the form of an

emulsion. The platelets were counted every five days for two months. As the results are important for the following discussion I will reproduce them graphically (Fig. 3). The values are averages of six platelet determinations on six different animals.

Bankow summarized his results thus: Castration, including ligation, is followed by a marked decline in the platelet value for about two months, after which the level rises but does not fully reach normal. This decline sets in more quickly after extirpation of the sex-glands than after ligation of their vessels, which is thought to be due to the fact that the sex hormones disappear suddenly in the former case, successively in the latter. Hyperhormonization elevates the platelet value immensely, with a maximum about the 35th day after the injection, whereupon the level falls and reaches the normal value at the end of the second month. To make sure that this was not a protein action, Bankow injected blood-serum in a control series (*d*). Here, too, he obtained an elevation of the platelet level, though of lower degree and of shorter duration. Bankow concludes that the changes he observed are due to a disturbance of equilibrium between the different endocrine organs of the body by respectively extinction and increased supply of sex hormones. The blood-platelet changes cannot be an effect of the diminution or increase of sex hormones *per se*, as after a time the platelet values nevertheless return to normal or thereabouts.

Bankow's interpretation of his results is open to some objections. If the diminution in platelets after castration is due to extinction of the sex hormones, the effect ought to assert itself sooner. The functional effect of castration on, say, the uterine musculature, can be observed as early as three or four days after the castration. Any hyperhormonization that may be produced by subcutaneous administration of two homologous sex-glands, crushed and emulsified in physiological common-salt solution, is undoubtedly very slight if any at all. The ovary itself contains a very small amount of hormone at any given instant, even during heat, and a hormonic effect is not conceivable for weeks from these dead, subcutaneously administered ovaries. The hypothesis that the increase or decrease observed by Bankow in the number of platelets was due to an increase or decrease of sex hormones is also in conflict with the fact that Kato, Benhamou and Nouchy, and I myself did not observe any alteration in the number of platelets in women after injection of known amounts of oestrin. There is a feature in

Bankow's curves to which he himself does not pay any considerable attention and which is rather obscured on account of his not counting the platelets oftener than every five days. All the three groups show initial rises of the platelet value. To this fact I am disposed to give an interpretation quite different from that of Bankow, to whose results I will return later.

On the basis of human material I have endeavoured to arrive at some idea as to whether the changes in the platelet curve during the monthly cycle can be related to the variations in the sex hormones during this cycle.

As is known, pregnancy is characterized by a very high oestrin titre, which attains its maximum at parturition or abortion. As soon as the placenta is detached from its maternal connexions, the folliculin titre falls very rapidly and reaches its normal value as early as within 10 days. I, therefore, studied the blood-platelet changes in a number of cases of parturition and abortion. The results are given in Fig. 4 and Fig. 5. These curves cannot lay claim to the same reliability as the menstruation curve in Fig. 1, as they are based on too limited a material. However, the changes in the number of platelets after parturition and abortion are so marked that these curves may none the less give an approximate idea. After parturition there is a rapid rise in the number of platelets to higher levels than are to be seen under any other conditions. The same is the case after abortion, although here the values do not fully attain the same height. As the period immediately following a menstruation coincides with an increase in blood-oestrin, and the period immediately after parturition and abortion with a much reduced blood-oestrin, it does not seem possible to put the analogous increase in platelets in both cases into causal relation with the follicular hormone. It appears more probable that another circumstance common to both occasions must be the cause of the increase in platelets. Comparison between the platelet curves after menstruation and those after parturition or abortion justifies the inference that the increase in platelets after menstruation cannot be causally related to the increased blood-oestrin during this time.

III. *What is the cause of variations observed in the number of blood-platelets during the menstrual cycle?*

Norman has studied the variations in the number of platelets after operations of various kinds. He finds that the organism responds to operative intervention with an increase in the plate-

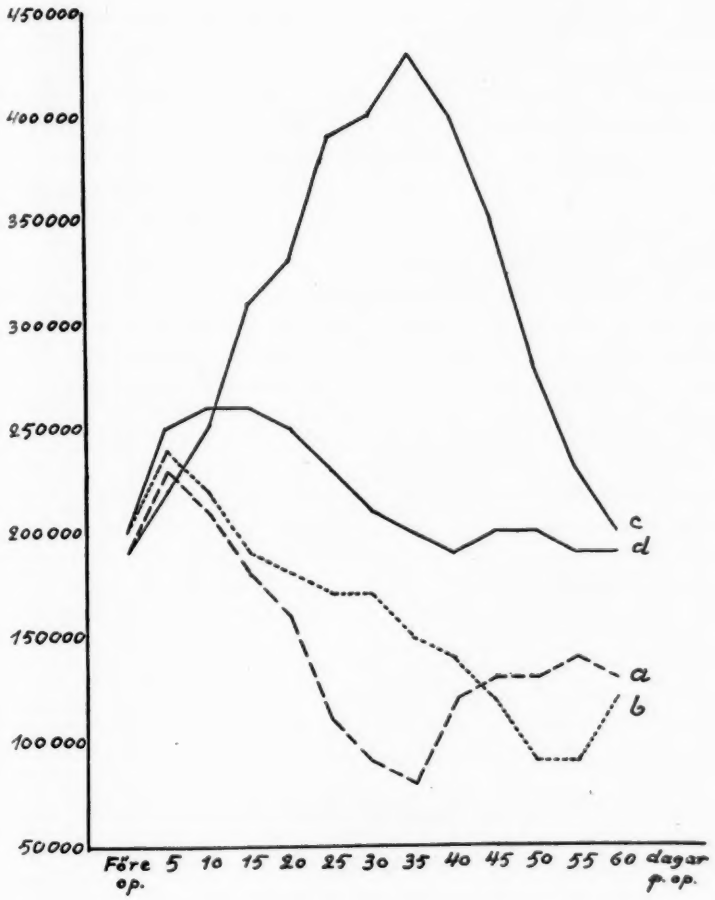
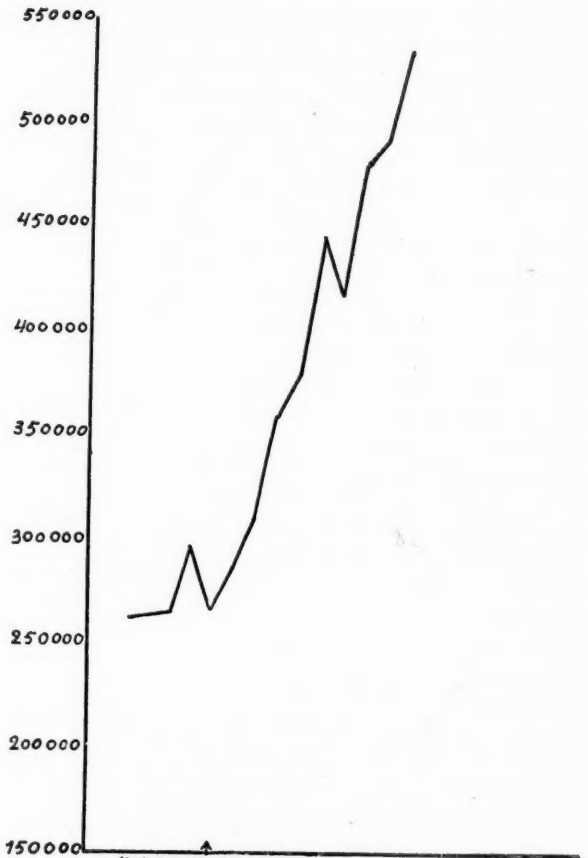


Fig. 3 (efter Bankow).



Trombocytantalets variationer efter partus.

17 fall

Fig. 4

lets, the chief cause of which must be in the operation itself. The narcosis and the extent of the haemorrhage are without influence. Norman considers the chief cause of this response of the organism to lie in resorption of blood, serum, and necrotic and thrombosed material. These substances are always at hand after an operation, as well as after accidents involving fractures and wounds, which likewise cause a rise in the blood-platelets. Windfeld[16] also has found a post-operative increase in platelets.

The findings of the authors mentioned have been tested by me in a small series of seven gynaecological laparotomies. The result is indicated in Fig. 6. The post-operative increase in the platelets is manifest.

It has accordingly been shown that an analogous increase of blood-platelets occurs after menstruation, parturition, abortion, and operation. And the explanation Norman is inclined to give of the post-operative increase appears also to be applicable with full validity to the increase in platelets after parturition and abortion as well as to that after menstruation. For in these latter cases there also, of course, occurs a resorption of blood, serum, and necrosed and thrombosed material. The lining of the uterus is a wounded surface after parturition and abortion as well as after menstruation, vessels are thrombosed, blood, serum and necrotic material are resorbed. Obviously the degree of this resorption must vary, being greatest after parturition and least after menstruation. It is then of interest to note that the degree of platelet-increase varies *pari passu*, greatest after parturition, least after menstruation. This fact appears to me to afford strong support for the view that the common cause of the increase in blood-platelets after parturition, abortion and menstruation lies in this resorption of necrosed material. In my cases I have not been able to follow the blood-platelet curves after parturition and abortion longer than nine days. As will be seen, the culmination here is not reached with certainity, and there is reason to assume that at least as long a time should elapse before the descending legs of these curves reach the normal value. Norman's post-operative curves allow of this assumption. It would then seem as if the increase in blood-platelets went on during approximately the time it takes for the re-forming of the mucous membrane to be completed, i.e. during the time the lining of the uterus is to be regarded as the surface of a wound.

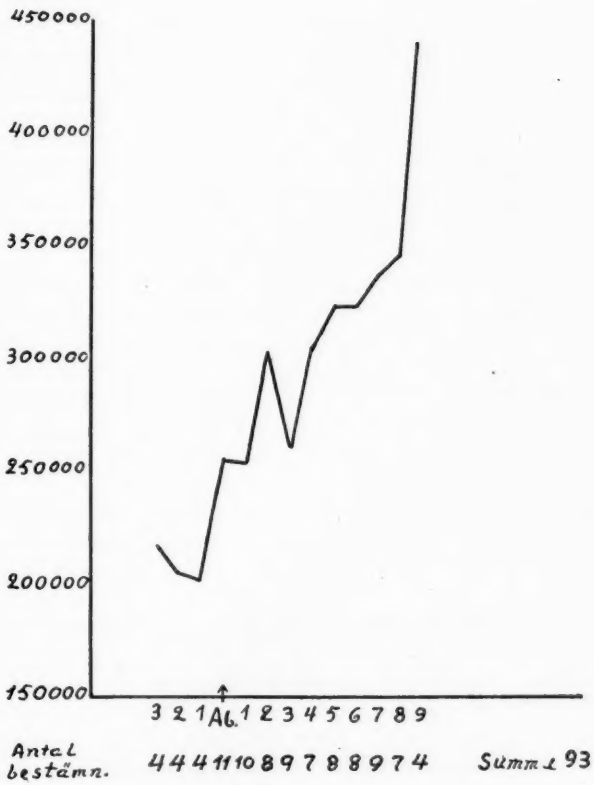
The resorption after an operation is not so easy to grade; it depends on both the extent of the intervention and the opera-

tive technique. Norman's curves, however, appear to show that major operations cause higher and longer rises in the blood-platelets than do minor ones. Norman's investigation and mine are thus mutually corroborative.

It seems to me that Bankow's curves ought to be viewed in the light of what has been said above. In all the test groups it was a question of an intervention: an operation, injection of blood-serum, injection of an emulsion of crushed ovaries or testicles. All the groups also show an increase in the platelets, of least degree and of shortest duration in the castrated groups (*a*) and (*b*), in which there must be the least resorption, and of somewhat higher degree and of longer duration in the blood-injection group (*d*), of highest degree and of longest duration in the group (*c*), in which a considerable amount of dead tissue was offered direct to the body's power of resorption, which is rather low in the subcutaneous tissue of rats on account of the poor vascularization. This may explain the excessively long duration of the platelet increase in this group.

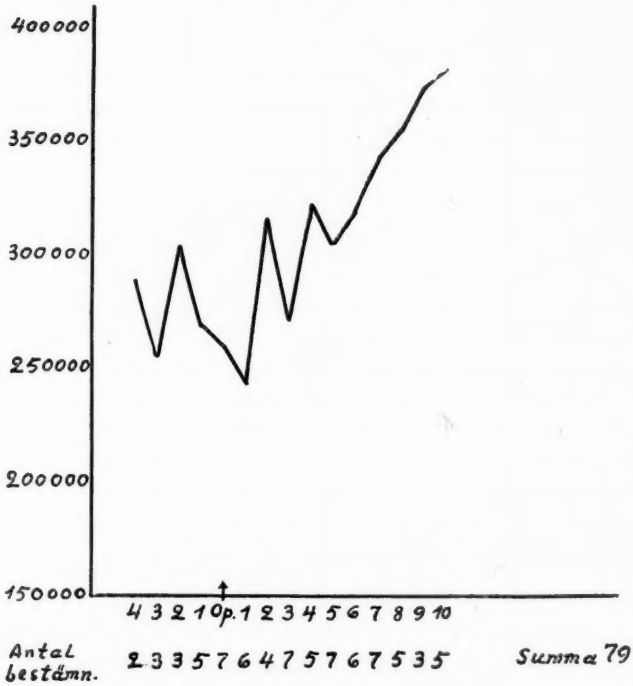
It, therefore, appears justifiable to consider that the increase in blood-platelets observed after menstruation is due to the organism's reaction to resorption of necrotic material.

While it is thus possible to advance an acceptable explanation of the post-menstrual increase in platelets, it is more puzzling to find one for the decrease in platelets observed at the onset of menstruation. Some attempts have been made to explain this sudden decrease. There has been an inclination to see in this a toxic reaction (menotoxin), or to explain it as an endocrine reaction via the spleen on the haematopoietic apparatus, to say nothing of other still more hypothetical attempts at explanation. I have hinted above at the possibility of correlating this sudden decrease in blood-platelets with the extinction of the corpus luteum hormone. The platelet curves after abortion and parturition (Figs. 4 and 5) show a similar initial diminution in the number of platelets before the characteristic increase begins. Now, here, too, it is of course possible to speak of an extinction of the corpus luteum hormone or at any rate of a hormone principle resembling that of the corpus luteum, in human beings linked up, at least in the latter half of the period of pregnancy, with the placenta. However, the post-operative platelet curve (Fig. 6) also discloses a similar initial decline, and this was also observed by Norman. That Bankow's curves (Fig. 3) do not indicate an initial decline of this nature is due to his not making platelet counts oftener than every five days. Since in these



Trombocytantalets variationer efter abort.
14 fall

Fig. 5



Trombocytantalets variationer efter operation.

7 fall

Fig. 6

latter cases there is not any parallel change in the concentration of the corpus luteum hormone, this fact contradicts the hypothesis in question. One way of definitely settling the question would be to trace the number of platelets in a series of cases in which the uterus had been excised but the ovaries left intact, cases with a sexual cycle but without menstruation. Cases of this kind are rare, however, and as there is also the difficulty of being able to follow them up for a sufficient time with daily platelet counts, such an investigation would require several years. For the present, therefore, I must abstain from any real attempt at an explanation. The fact remains that the number of blood-platelets suddenly diminishes on the first day of menstruation, but the cause of this and its physiological import are unknown.

SUMMARY.

The author has studied variations in the number of blood-platelets during the normal menstrual cycle, 1,433 determinations being made on 38 women. The number of platelets varies in a typical manner. On the first day of menstruation there is a fall in the number of platelets from about 230,000 per c.mm. to about 200,000. During the first 10 days of the cycle there is a slow rise in the number of platelets, the culmination being reached about the 11th day with about 265,000 per c.mm. From the 11th to about the 21st day the number slowly declines to about 230,000. During the last week of the cycle the number remains constant at 230,000 until the sudden diminution occurs at the onset of menstruation.

These variations are not, as has been presumed, due to variations in the concentration of the follicular hormone. The author shows that a similar increase in platelets occurs after parturition, after abortion, and after operation. As the change in the concentration of oestrin after parturition and abortion is quite the reverse of that after menstruation, and the oestrin can have no connexion with post-operative changes, it is not possible to regard the post-menstrual increase in platelets as standing in a causal relation to the hormone of the follicle.

The question whether the sudden decline in blood-platelets at the onset of menstruation stands in a causal connexion with the extinction of the corpus luteum hormone that takes place at this time is left open for the present. It cannot be settled on the basis of the present material.

The author is inclined to explain the analogous increase in platelets after menstruation, parturition, abortion, and operation

as a reaction of the organism to resorption of necrosed material and finds this explanation corroborated by the fact that the degree and duration of the platelet increase on these different occasions occur *pari passu* with the degree and duration of the resorption.

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Recent Findings in Solid Ovarian Tumours.*

BY

WALTER SCHILLER, Vienna.

IT is not without justification that the chapter on ovarian tumours is considered one of the most difficult in gynaecology and pathology. Primarily great difficulties arise in the aetiological examination of the ovarian tumours. Until quite recently there has not been any clear conception from which part of the ovary some of these tumours arise. The uncertainty of derivation led to a lack of lucidity in the classification so that up to the present day a uniform system does not exist. Every textbook gives a different division. Paralleling these pathological difficulties are the clinical difficulties in the prognostic significance of ovarian neoplasms. Opinion varies as to whether one special ovarian tumour or a whole group of ovarian tumours is to be considered as benign or malignant. This latter uncertainty is far worse than the lack of clearness in histological and pathological understanding, for it causes an indefinite therapy and there is possibility of grave errors. It would be an error if the necessary total extirpation and radiation after-treatment were omitted because the malignant tumour was taken for a benign one. This mistake is made comparatively seldom. In certain tumours, according to the literature, benign neoplasms are considered malignant, not too rarely, with disastrous results. Young women or girls with unilateral benign ovarian tumours have been castrated by operation or radiation therapy and unnecessarily maimed for their entire lives, because the structure of these tumours has been mistakenly considered malignant. Such errors can be avoided if the operator and the pathologist who examines the specimen are familiar with the structure and clinical significance of the tumour in question.

The fact which makes our study of ovarian tumours so difficult is that the tissue of which they consist differs greatly from the tissue of the organ in which they develop, viz. the ovary. Generally, it is possible to see from the character of the tumour tissue where it arose. The fibroma develops from

* Lecture delivered at the British Postgraduate Medical School, London, October 17th, 1935.

connective tissue, the lipoma from lipoid tissue, the epithelioma from epithelium. Thus each of these tumours corresponds, as far as its cellular character is concerned, with the tissue from which it arose and from which it developed. With the ovary, however, this is altogether different. There are a number of neoplasms, the cellular elements of which have no analogue in the tissues which help to build up the ovary. The pseudo-mucinous cystoma, the disgerminoma, and the serous cystoma, for example, consist of cells which do not exist in the normal ovary. Therefore, we cannot find within the area of the tissues, which form the normal ovary, the tissue from which these tumours arise. The only exception is the fibroma to which the stroma of the ovary corresponds and the granulosa-cell tumour to which the follicle corresponds. For all the other tumours of so-called heterotopic tissues we must find a special explanation as to how the heterotopic tissue of origin came into the area of the ovary. In former times for pathogenetic reasons the derivation from the ovulum or from spread misplaced embryonal germs was generally believed, and thus all tumours in question were given teratoid character in a certain sense. This process did not hold good and did not bring the necessary lucidity in the classification of ovarian neoplasms. Our present improved information and knowledge of the derivation and clinical importance of a part of the ovarian tumours is, in the first place, due to the progress which embryology has made in the course of the last 10 years. The concepts of embryogenesis of the ovary have changed more than that of any other organ. Our ideas of the ovulum and of the granulosa, the two most important parts of the ovary have changed completely. It was formerly believed that the ovula arise from the surface epithelium, i.e. that their anlage is primarily in the area of that part of the coelomic epithelium which covers the surface of the ovary. Nowadays we know that this assumption was wrong, and that the germinal cells develop in the dorsal part of the primordial gut and by the way of the germinal route passing the mesenterium they invade the gonad from the hilus. As to the granulosa, the idea was formerly dominant that it arose from projections and proliferations of the surface epithelium. It was believed that the surface epithelium forms the germinal cords and from the cells of the germinal cords the granulosa was supposed to develop. Fischel demonstrated that the predominant part of the germinal cords develops from differentiation of the mesenchymal core of the gonad. As Grünwald proved, only a small part arises indeed

from the surface epithelium in the form of the so-called secondary germinal cords; this was formerly believed to be the point of origin of the granulosa. These secondary germinal cords form in the testis a somewhat larger part of the parenchyma. In the female sexual gland they do not play an essential *rôle*. Thus we see that the granulosa is primarily of mesodermal and mesenchymal origin. The same holds for the male germinal cords, especially the sertoli cells. The statement that the ripe epithelial granulosa arises originally from mesodermal tissue and only secondarily differentiates into epithelial forms makes it clear that tumours of this tissue, when unripe, have the character of connective tissue and, when mature, show epithelial structure. Tumours which have ripe and unripe parts will offer the picture of a combination of parts of epithelium and parts of connective tissue. Such structures were formerly mistakenly explained as sarco-carcinomata or carcino sarcomata.

Following the origin of the gonad there is an undifferentiated mesenchyme into which the germinal cells enter from the primordial gut. This mesenchyme is histologically undifferentiated, yet each single cell possesses male or female characteristics in its chromosomes. Thus, that parenchyma is histologically undifferentiated yet cytologically sexually determined. In the embryonic ovary where it is determined in the female direction it possesses the latent prospective potency to form granulosa. In the embryonal testicles where it is chromosomatically determined in the male sense, it has the prospective potency of forming germinal cords, i.e. sertoli cells. So far as the ovary is concerned the stimulus for the differentiation is the invading primordial germ cell. The normal mechanism is as follows: (*a*) Mesenchyme determined in the female direction, invading ovula, differentiation of granulosa; (*b*) Mesenchyme determined in the male direction, invading spermatogonia, differentiation of sertoli cells.

This normal mechanism may be disturbed in three different ways.

(*a*) Normal female parenchyma cells remain as embryonic relics and many years later an unspecific stimulus causes their activation in their original inherent direction and they develop granulosa-cell tumours.

(*b*) By malformation cells determined in the male direction are formed in the parenchyma of the ovary otherwise determined in the female line. They remain as embryonic relics and only years later do they develop upon an unspecific stimulus their prospective potentialities to form male germinal cords or

testicular channels. But, of course, these tumour-like testicular channels are without spermatogonia. We call these tumours for their masculinizing effect based on hormonic influence arrhenoblstomata.

(*c*) By cellular malformation, in the otherwise normally differentiated mesenchyme of the ovary, cells are formed which are determined neither in the male nor in the female line, but are neutral. Such neutral cells may develop in the ovary as well as in the testicles and then may remain dormant as foetal remnants. Later on they may develop tumours of mostly alveolar structure without hormonic effect in either sex gland. At first given the names of large cellular carcinoma or sarcoma, later on seminoma, and, finally, they are called disgerminoma. They develop in the ovary and in the testis, and have no hormonic influence.

The disturbance in mechanism is: In ovary only (*a*) normal female parenchyma cells left as embryonic relics develop granulosa-cell tumours; (*b*) pathologically male determined parenchyma cells left as embryonic relics develop arrhenoblastomata. In ovaries, testicles, or hermaphrodite gonads: (*c*) pathologically neutrally determined parenchyma cells left as embryonic relics develop disgerminoma.

Granulosa-cell Tumours.

These develop from relics of the normal mesenchymal core of the ovary, never as formerly believed from the granulosa of the already mature follicle. That granulosa-cell tumours develop from the granulosa of ripe follicles could not be proved and, therefore, that conception receded into the background. We rather infer that during the embryogenesis of the ovary parenchymal remnants which did not enter into any relation with the ovulum were left there. Years later, due to an unspecific stimulus in these cells, their inherent tendency of forming female germ cords shows itself. First, a cellular parenchyma develops by proliferation and offers an aspect very similar to a cellular fibroma. Gradually trabeculae which correspond to germinal cords develop from this cellular tissue. Yet the ovula which would normally be the guiding influence are missing and, therefore, an irregular tumour network develops instead of parallel germinal cords. The trabeculae are at first composed of connective tissue and do not show any sharp demarcation from the surrounding stroma. Later on with increasing maturity of tissue they become epithelialized and become sharply demarcated from the stroma: as ripe

trabecular forms. Perfectly formed ripe cellular material begins to proliferate in tumour-like fashion and forms larger masses of tumour parenchyma which are separated from each other by narrow septa-ripe soid forms. Finally the parenchyma forms follicle vacuoles filled with liquid, as does the granulosa. The only difference is that since ovula are not present the cavities are irregular in shape and distribution. We call this form ripe follicular, or folliculoma. In the mature form of granulosa-cell tumours there are often the so-called Call-Exner bodies to be seen. (Fig. 1). These formations were formerly explained incorrectly as new-formed ovula or nutritive channels. It is to the great merit of Thomson, who proved in his classical but insufficiently appreciated investigations on the histology of the normal ovary that the Call-Exner bodies develop by hydropic degeneration of single cells. They are characteristic for granulosa but not specific. In most granulosa-cell tumours of high maturity low maturity parts of tissue are found in the border areas, the ripening process beginning in the centre and progressing toward the periphery. The riper a granulosa-cell tumour gets the more it acquires the hormonic function of the ripe granulosa and soon forms folliculin. This formation of folliculin parallels another function of the ripening physiological follicle, namely the prevention of ripening and bursting of follicles. Therefore, ovulation does not occur, and consequently menstruation does not occur. This primary amenorrhoea is an important sign in young women and girls. On the other hand, the folliculin causes an hypertrophy and hyperplasia of endometrium which, by casting off the hyperplastic oedematous layers of the superficial mucous membrane, may lead to irregular haemorrhages from the enlarged capillaries. These irregular bleedings, metrorrhagia, are the foremost clinical symptoms in elderly post-climacteric women, in whom not infrequently granulosa-cell tumours are seen. That granulosa-cell tumours may occur in old women is evidence against the conception of the development of granulosa-cell tumours from the granulosa of follicles. Elderly women after the climacterium do not have any follicles and consequently no granulosa. There is no doubt that granulosa-cell tumours cannot primarily develop from the genuine granulosa of the follicles.

It is definitely certain that granulosa-cell tumours are primarily benign and in the great majority unilateral. They are generally round with a smooth surface. Their parenchyma is, in unripe forms, more of the fibrous type; in the ripe ones it is more

homogeneous and softer. They frequently show larger cystic vacuoles and are inclined to haemorrhagic degeneration in their ripe forms. Presumably malignant granulosa-cell tumours also exist. Sometimes bilateral cancers of the ovary occur, the structure of which resembles granulosa-cell tumours. So far the morphological resemblance is concerned these carcinomata may be considered as granulosa-cell tumours degenerated to malignant type. But it should not be forgotten that other cancers of the ovary which primarily were cystic and papillary may also develop structures similar to granulosa cells. Therefore, the diagnosis, malignant granulosa-cell tumour, can only be given problematically, not with full certainty. In such cases it it advisable to make the diagnosis of malignancy from the polymorphous nature and lack of conformity of the cells and to declare the origin from a granulosa-cell tumour as probable. If, however, in such neoplasms cells are seen which never occur in the granulosa as high cylindrical cells secreting mucus, then the derivation from granulosa may be excluded.

Arrhenoblastomata.

Cells of the mesenchymal part of the ovary are pathologically of the male type and have consequently the inherent tendency to form germinal cords. If these remain as embryonic rests and later on are made to proliferate by some unspecific stimulus tumours develop which imitate the development of the foetal testis but without spermatogonia. The frst phase is marked by the trabeculae becoming differentiated irregularly from cellular connective tissue. At this stage the tumours closely resemble granulosa-cell tumours of immature stage. Yet the trabeculae of granulosa-cell tumours consist of several layers of round cells, while the arrhenoblastoma consists usually of two or three layers of long cells, the axes of which are vertical to the direction of the trabeculae. In their maturer forms these trabeculae show a tendency toward forming a lumen similar to that of the male cords. However, these are never seen in the area of granulosa. The mature arrhenoblastoma shows small narrow anastomosing channels just as the foetal testis does. In the earliest stages interstitial cells loaded with lipoid, the so-called Leydig cells, develop in the testicle and similar cells are to be seen in arrhenoblastoma. They are a further characteristic for differentiation from granulosa-cell tumours. (Figs. 2 and 3).

The arrhenoblastoma produces a male sexual hormone which has a masculinizing effect on the patient. The essential signs of

masculinization are abnormal growth of hair of male type on the face and body; the voice grows deeper, adopting a male character and then the clitoris takes on the form of a small hypospadic penis. The signs of masculinization subside as a general rule after extirpation of the arrhenoblastoma, only the voice cannot return to its former pitch since the enlarged masculine larynx is unable to return to the female shape. The masculinizing effect of the arrhenoblastoma is connected with certain potentialities in the organs, and not all women possess these potentialities. They are remnants of a primarily bisexual anlage which disappear in some individuals and persist in others. Evidence that there are women without such an anlage and that the masculinization by an arrhenoblastoma is dependent on the presence of such anlagen is given by the fact that there exist typical arrhenoblastomata whose hosts do not show any vestige of masculinization.

The arrhenoblastoma is nearly always unilateral and primarily benign. Malignant cases are rare exceptions. Macroscopically the arrhenoblastoma looks exactly like a granulosa-cell tumour. It is hardly possible to distinguish them from one another with the naked eye.

Disgerminoma.

If cells of the mesenchymal cord remain quiescent in a sexual gland, be it an ovary or a testis, and, if by a form of chromosomal malformation they are not determined sexually (neuter), they may develop later into tumours of a peculiar histological character. A strong point in favour of this derivation of the disgerminoma is the fact that the greatest part of these none too rare neoplasms which develop in hermaphroditic gonads are disgerminomata. In a sexual gland determined half female and half male the development of neutral parts is very probable. The disgerminoma consists of large cells with vesicular round nuclei and narrow light protoplasm. It is characteristic of these cells to shrink most easily, especially when quickly embedded in paraffin. A proper picture of the structure is only obtained by making frozen sections or embedding the tissue in celloidin. These large round cells are either lying in small alveoli or in narrow strips in the stroma. In former times the alveolar form was frequently called the alveolar large-celled sarcoma or carcinoma of the ovary or testis (Figs. 4 and 5). It is typical that the connective tissue of the septa in these neoplasms is nearly always diffusively infiltrated with lymphocytes; small foci of epitheloid

cells as well as giant cells of the Langhans type are frequently to be seen. In this way the picture of tuberculosis is imitated. An exact examination will prove, however, that the giant cells do not lie in the form typical of tuberculosis in the centre of the focus but often outside and even isolated between the tumour cells. A fat staining will reveal profuse lipoid droplets in the protoplasm of the giant cells. Evidently the tissue of disgerminoma when decaying produces a lipoid substance which causes a reaction in the tissue similar to tuberculin so that granulation tissue develops which bears the morphological character of tuberculous granulation tissue (Fig. 6).

The disgerminoma occurs both in women and men, yet there are two important points of difference. In the ovary it occurs mostly in young individuals, the majority of disgerminomata develop between the 13th and the 20th year. In men disgerminomata very rarely occur before the 40th year. The second point of difference lies in the prognosis. The disgerminomata of young girls is benign in a high percentage, 70 to 90, of cases. The disgerminomata of men is malignant in nearly all cases. The majority of disgerminomata in women are bilateral; according to recent statistics more than half of them. They are massive, predominantely kidney-shaped neoplasms with smooth surface and rather soft consistence. On section yellowish staining shows the lipoid degeneration. The disgerminomata do not have any hormonic influence but we can often see that the patient with a disgerminoma will show symptoms of hypoplasia and infantilism. It must be emphatically stated that most of the unilateral disgerminomata are benign. That is why one is not justified in performing a total extirpation when such a disgerminoma has been diagnosed in a young girl, or to add radiation therapy with the resulting castration of the patient. We can refer to a series of cases of young women who had unilateral disgerminomata removed without total extirpation and without radiation after treatment and in whom pregnancies later occurred. Cases of patients who, after a simple extirpation of a unilateral disgerminoma, had perfectly normal sexual functions and continued to be in perfect health prove the fallacy of radical therapy based upon an unjustified diagnosis of malignancy.

Brenner's tumour.

The following tumour is altogether different from the above-mentioned three neoplasms, which further demonstrate their close relation to each other by the fact that they occur combined not

too rarely. The so-called Brenner tumour received its name from Brenner who described it erroneously in 1907 for the first time; for he gave it the name of oöphoroma folliculare. Yet the assumption that Brenner was the first to see and describe this tumour is in reality incorrect. E.G.Orthmann described in 1899 such a tumour as fibroma papillare superficiale carcinomatosum. An excellent description with all the symptoms of the tumour was given by Fothergill and Donald in *Journal of Obstetrics and Gynaecology of the British Empire*, 1902, ii, 15-20.

The Brenner tumour consists of three different elements: (1) of fibrous proliferated connective tissue into which (2) small islets of unripe solid squamous epithelium have grown. These islets contain (3) inclusions of high pseudomucinous cylindrical epithelium. These latter inclusions which often adopt a cystic or glandular character may be missing, yet this does not change the diagnosis of Brenner's tumour (Figs. 7 and 8). The Brenner tumour does not arise from the mesenchymal core of the ovary. The combination of both of the epithelial elements is normally in the region of the urinary system. In the pelvis of the kidney as well as at the mouth of the urethra normally transitory epithelium is adjacent to high cylindrical epithelium. (Fig. 9). In these regions inclusions of glandular epithelium in layered transitory epithelium will normally occur at times. We may presume that Brenner's tumours develop from the dislocation into the gonad of germs which primarily belonged to the urinary system. This concept is backed by the fact that Brenner's tumours develop frequently in the hilus of the ovary. I was able to show in one case that a Brenner tumour developed from the rete ovarii, that is, from the site of the primary urogenital connexion. Similar prospective potentialities as in the tissue of Brenner's tumours are occasionally to be seen in the surface epithelium of the ovary and in the serosa of the Fallopian tube and round ligaments in the shape of nodules of squamous epithelium with glandular inclusions.

The Brenner tumour usually develops only small nodules varying from the size of a pea to that of a chestnut; larger Brenner tumours are rather rare. The small nodules are most often found in the wall of cystomata, the pseudomucinous cystoma being the most common, and in dermoids. The Brenner tumour, not having any hormonic effect whatever, is almost impossible to diagnose clinically. The small nodules escape detection, and the large neoplasms are clinically similar to fibromata. The malignant degeneration of Brenner's tumours has been described, yet if that

really does occur it must be considered as one of the rare exceptions. It is worth mentioning that the glandular inclusions have a strong tendency to degenerate; the epithelial cells flattening greatly, a colloid-like round droplet remains in the lumina of the glands, which becomes stained deeply with eosin. Such structures were often formerly considered primordial ovula and consequently the tumour was diagnosed as oöphoroma (Fig. 10).

Xanthofibroma thecacellulare.

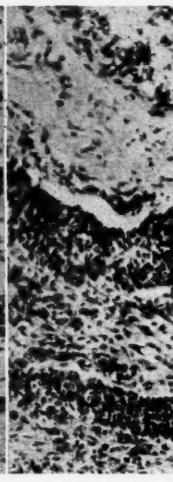
Another ovarian neoplasm which has been discovered in the last few years and has been investigated and discussed in only few publications is the so-called xanthofibroma thecacellulare, which was described for the first time by Löffler and Priesel. The exanthofibroma is an unripe cellular fibroma which is permeated by small lipoid droplets. These droplets change the colour of the xanthrofibroma—which otherwise, as far as consistence and structure is concerned, does not differ from an ordinary fibroma—in such a way that on section it has a yellow sometimes yolk-like colour (Fig. 11). A xanthrofibroma if fixed in formalin and then left in a solution of Sudan will become stained diffusely red, so that according to the description of the discoverers it has the appearance of a tomato.

Clinically the xanthofibroma causes the same mechanical symptoms as an ordinary fibroma. Yet the fat which it produces and stores, having an hormonic character, may at times cause hyperplasia of the mucous membrane with bleeding. Amenorrhoea can also occur because the elements of the tumour are luteinized connective tissue of the ovary. They are related to the physiological theca. That is the reason why Löffler and Priesel for better description added to the name xanthofibroma the attribute thecacellulare. Xanthofibroma thecacellulare occur in young and elderly women. They vary in size from that of a hazel-nut to that of a fist. The clinical symptoms correspond to a combination of fibroma in the mechanical way and to granulosa-cell tumours in the horminic way.

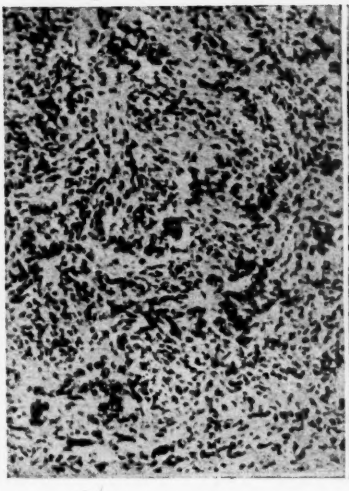
Immature solid

Immature trabecular

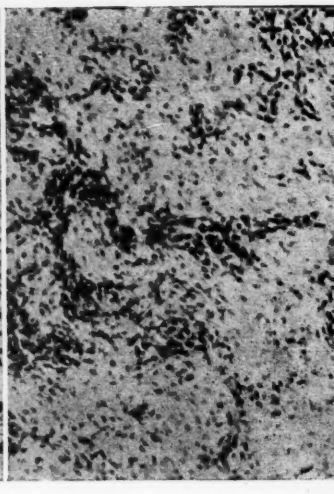
Mature t



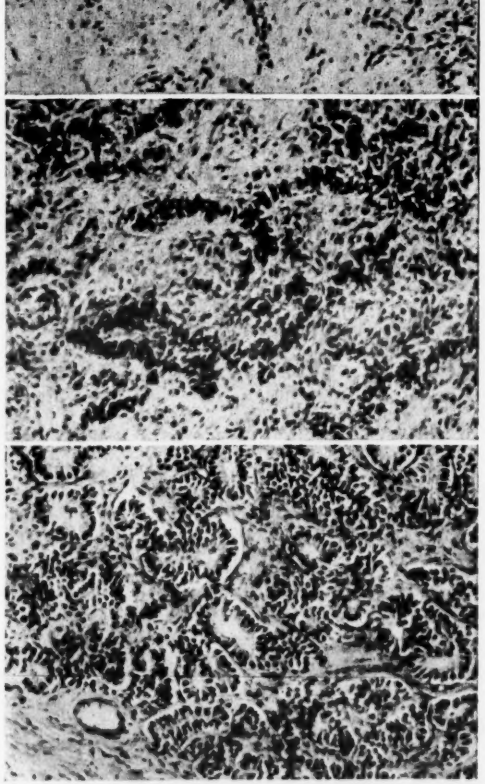
Immature solid



Immature trabecular



Germinal cords
testicle embryo,
19 mm.

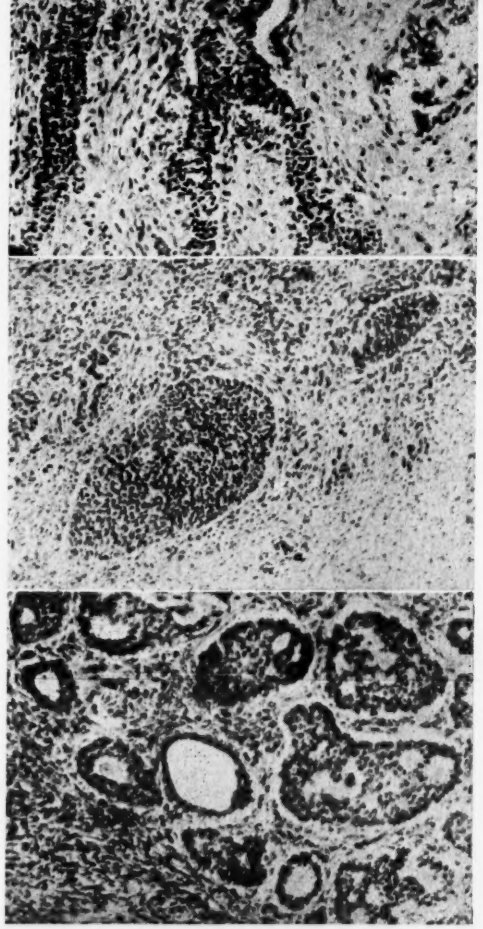


Mature trabecular

Mature trabecular

Mature canalicular

FIG. 2.
Development of arrhenoblastoma.



Mature trabecular

Mature solid

Mature folliculoid

FIG. 1.
Development of granulosa-cell tumour.

UNIV. OF WICH.

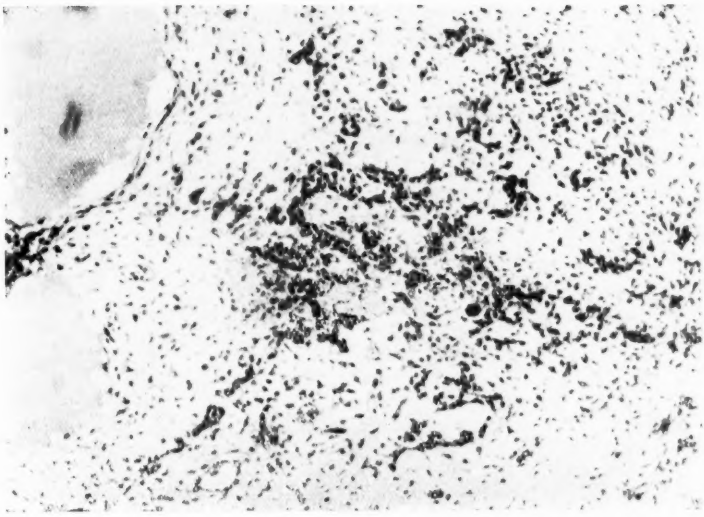


FIG. 3.

Arrhenoblastoma. The strip in the centre shows beginning canalization.

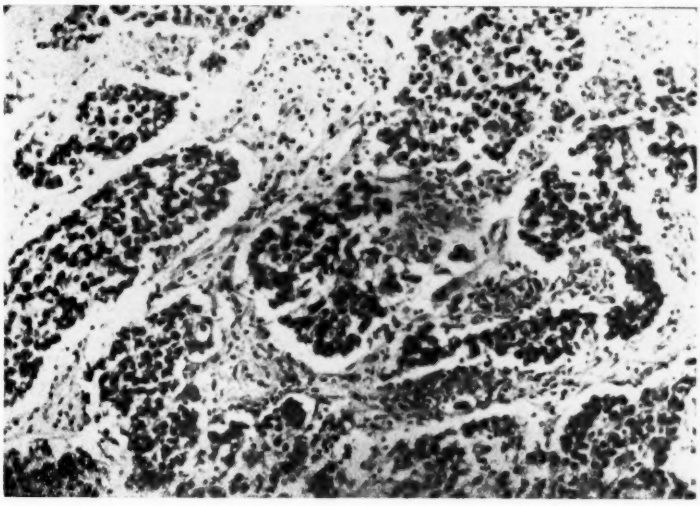


FIG. 4.

Disgerminoma. (Paraffin slide)

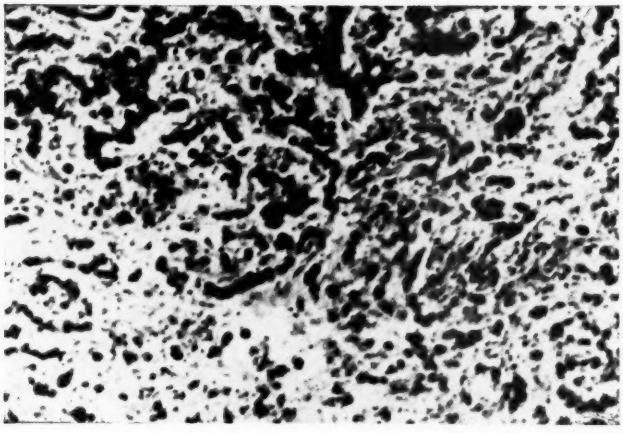


FIG. 5.
Disgerminoma (frozen slide).

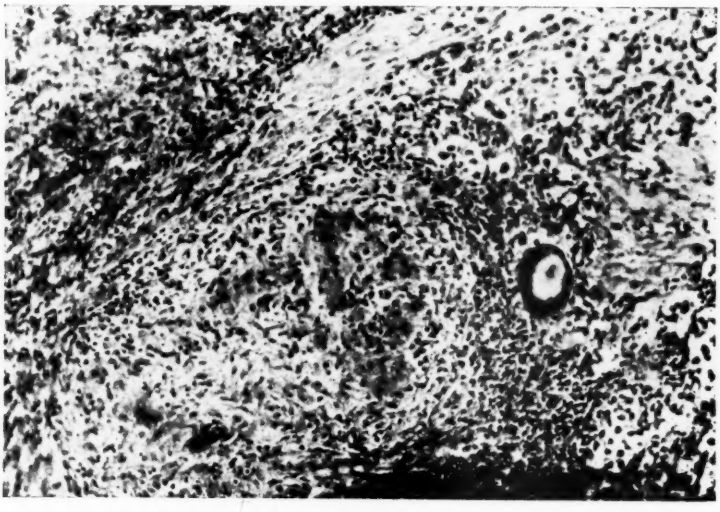


FIG. 6.
Disgerminoma. Pseudo-tubercle.

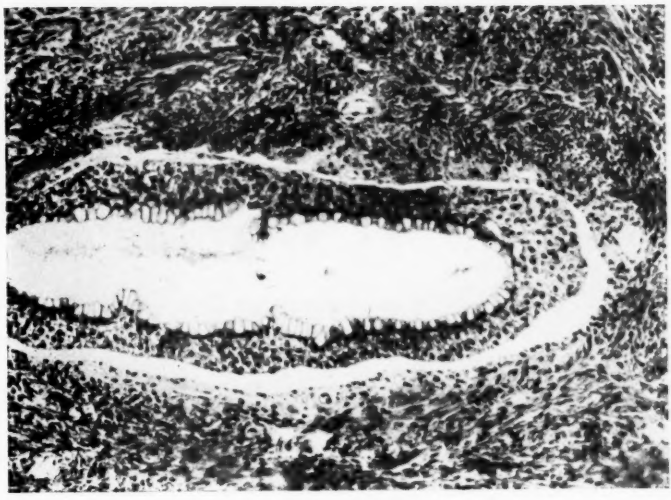


FIG. 7.
Typical Brenner tumour.

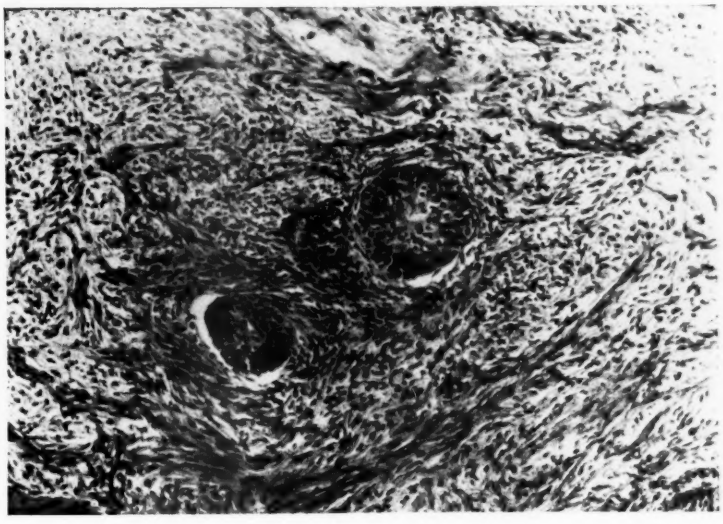


FIG. 8.
Brenner tumour. No columnar epithelium.

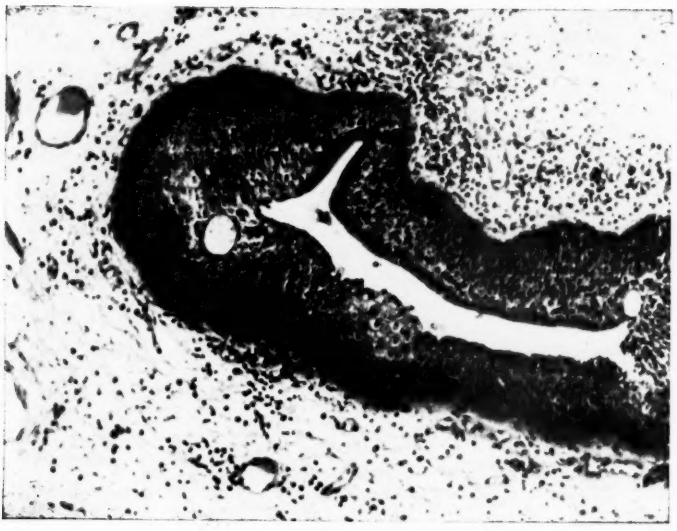


FIG. 9.

Opening of urethra. Projection of mucous membrane. Stratified epithelium surrounding mucinous gland.

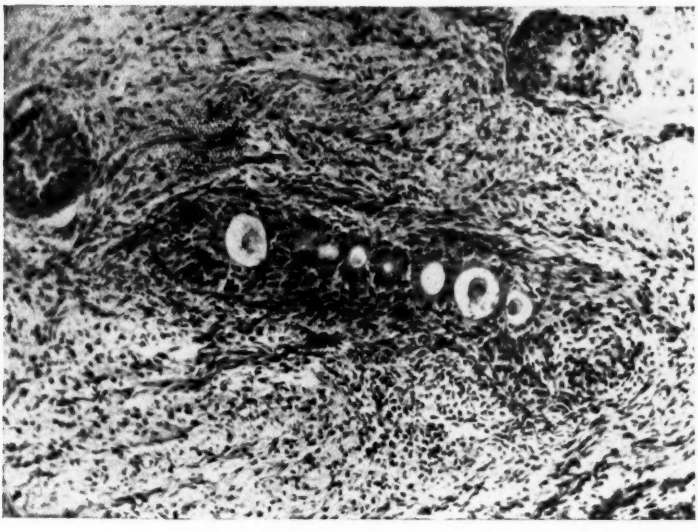


FIG. 10.

Brenner tumour. Pseudo-ovula.

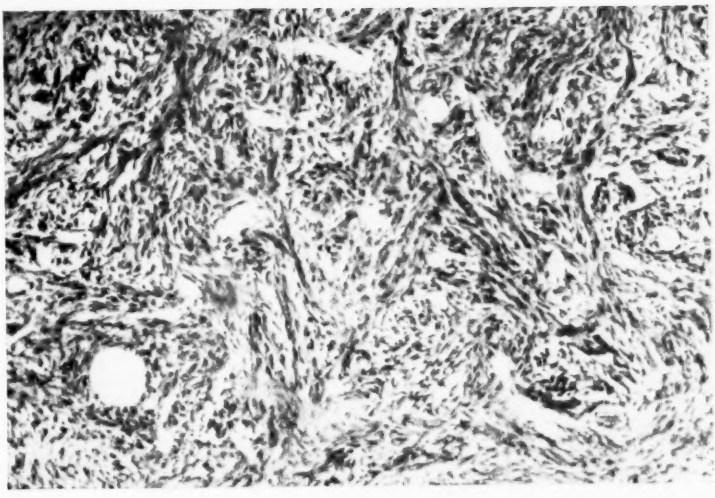


FIG. 11.

Xanthofibroma thecacellulare.

A New Ergot Preparation : Ergometrine.*

BY

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(Director: Prof. E. Hauch, M.D.)

"IT is our opinion that the ergot problem has now been finally solved." This is the tenor of the concluding statement of an article by four Americans, Adair, Davis, Kharasch, and Legault,[1] recently published in the *American Journal of Obstetrics and Gynecology*. This work deals with clinical experiments with a hitherto unknown water-soluble substance found in the fungus *Claviceps purpurea*, or *Secale cornutum*.

The honour of discovering the presence of this new oxytoxic substance is due in the first place to the young London gynaecologist, Chassar Moir.[2, 3, 4] From a series of investigations conducted during the years 1932–34 into the action of various preparations of ergot he arrived at a result entirely contrary to the prevalent opinion held formerly. It had been held that the action of ergot was first and foremost due to the presence of the so-called ergot alkaloids, ergotoxine and ergotamine. Moir now found that he could, on the contrary, produce a powerful effect on the uterus with various ergot preparations extracted in such a manner that practically not any ergotoxine or ergotamine was contained in them. Moreover, some of these extracts had been kept so long that any trace of these alkaloids must long since have been converted into inactive decomposition products. The results showed that ergot must still contain an active component, the presence of which had escaped the notice of the many investigators who had previously been engaged on the ergot problem. In consequence of these findings a new chemical investigation of ergot was undertaken by the late Dr. H. W. Dudley who, working in co-operation with Moir, succeeded in isolating the new active principle, to which the name ergometrine was given. On March 14th, 1935, Dudley and Moir[5] made their first announcement, in the *British Medical Journal*, of the

* A lecture given to the Gynaecological and Obstetric Society, Copenhagen, on December 13th, 1935, by E. Möller-Christensen.

production of ergometrine and mentioned certain characteristic chemical properties by which it differs from the ergot alkaloids.

Ergometrine has since been produced elsewhere. Kharasch and Legault were the first to do so in America, where they gave it the somewhat unfortunate name of ergotocine (which can very easily be confused with ergotoxine). In the work quoted at the beginning of this article they give, in co-operation with Adair and Davis, a further account of the chemical and biological properties of ergotocine, to which brief reference will now be made.

It is a colourless crystalline powder consisting of very long and thin crystals. It dissolves very easily in water but with difficulty in chloroform. Its melting-point begins at 155°F. and ceases at 160°F. Its empirical formula is stated to be $C_{21}H_{27}N_3O_3$.*

The toxic effect of the substance is extremely light. Karasch and Legault found that the smallest lethal dose for a mouse was 250 mg. per kilogram, and the smallest lethal dose for a guinea-pig 80 mg. per kilogram body-weight. Two dogs, which were given one milligram of ergotocine intramuscularly daily for 20 days, did not display any toxic symptoms. Finally, they have shown that, even in very large doses, it has no effect on the blood-pressure or urine secretion of human beings, as is not the case with pituitrin.

Before proceeding to give an account of our own experiments, mention will be made of the fact that Stoll produced a water-soluble oxytocic substance from ergot a few months ago, which he called ergobasine. Since this paper was written it has been agreed that both ergobasine and ergotocin are identical with Dudley's and Moir's ergometrine.[7]

The preparation with which our experiments were carried out was prepared at our request by the Löven Chemical Factory, Copenhagen, in accordance with instructions laid down by Dudley and Moir in their first work.

It is a white crystalline powder (see Fig. 1) easily dissolved in water but with difficulty in chloroform. Its melting-point is about 150°F. A most essential point is that it is in photometric agreement with Dudley's preparation. We have no doubt that it is identical with this latter and, therefore, also use the name ergometrine.

* In a more recent work Dudley[6] has shown that ergometrine has the empirical formula $C_{19}H_{23}O_2N_3$. It is probable that the formula $C_{21}H_{27}O_3N_3$ attributed to the new substance by Kharasch and Legault is inaccurate.

FIG. 1.

Ergometrine crystals. (Microphotograph).

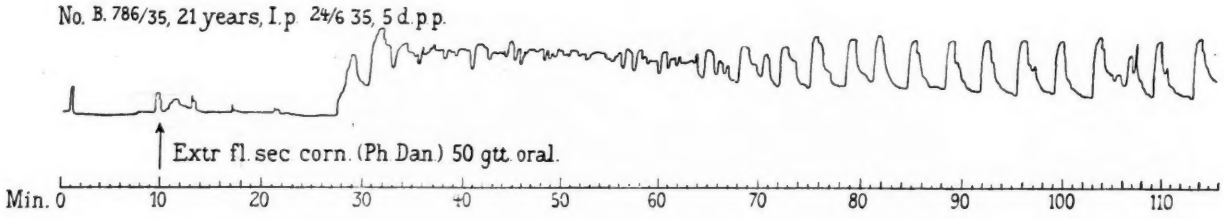

FIG. 2.

Tracing made the fifth day post-partum by the extra-abdominal method. 50 drops extractum fluidum secalis cornutum (Ph. Dan.) was given by mouth. Effect about 20 minutes later.

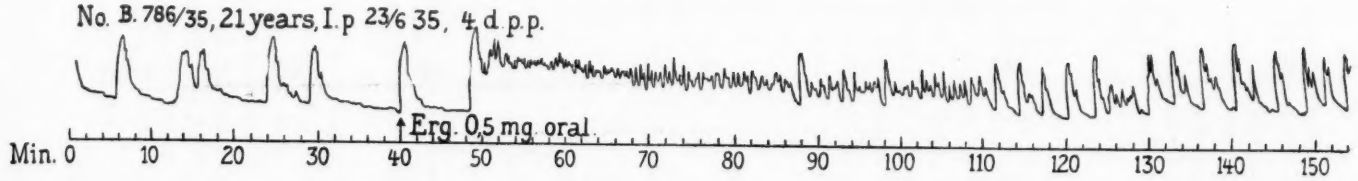

FIG. 3.

Tracing made the fourth day post-partum by the extra-abdominal method. 0.5 milligram ergometrine (Dan.) was given by mouth. Effect 10 minutes later. The same person as Fig. 2.

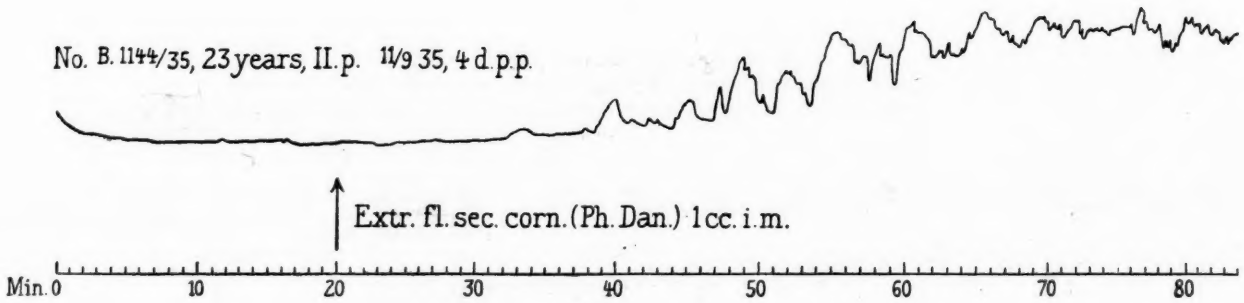

FIG. 4.

Tracing made the fourth day post-partum with the external apparatus, showing the effect of 1 c.c. extractum fluidum secalis cornutum (Ph. Dan.) by intramuscular injection.

The dosage is somewhat dependent on the manner in which the substance is administered. By the mouth, 0.5 mg. tablets are given. For rectal injection, one 0.5 mg. tablet is dissolved in a little water. Intramuscularly, a dose of 0.25 mg. is given dissolved in 1 c.c. of physiological salt solution, and intravenously 0.1 mg. dissolved in 5 c.c. of physiological salt solution. There is no objection to the same dose being repeated after an interval of from 5 to 10 or 15 minutes' interval, should it be considered necessary.

Within certain limits the intensity of the action of ergometrine is directly proportional to the size of the dose. This applies to the "strength" (if this expression can be used) of the contraction of the uterus as well as to its duration.

With doses such as we have given, and which we consider may be taken as therapeutic doses, the action falls into two phases. (1) In the first phase a tonic, or tetanic, contraction of the uterus is predominant, though frequent small rhythmic contractions also take place. We call this phase the tonicoclonic stage. It changes gradually to (2) the second phase, which we call the clonic stage. Here powerful contractions are seen to follow one another in rapid sequence, while each is succeeded by a complete relaxation of the uterus. This phase slowly passes away and the uterus slowly returns to the same rhythm of contraction as before the administration of ergometrine.

The duration of the two stages is, as has already been mentioned, dependent on the size of the dose. This applies especially to the tonicoclonic stage, which may be quite imperceptible if the dose has not been sufficiently large. We furthermore found that the tonicoclonic stage lasted from 45 to 90 minutes.

The clonic stage lasts for several hours. In one particular case we examined the uterus six hours after the oral administration of 0.5 mg. of ergometrine and found that the clonic stage still continued.

Patients can stand ergometrine in the doses we gave quite well. We never observed nausea, vomiting, or any other unpleasant side-effect; nor have we observed that the blood-pressure had been affected. We registered the contractions of the uterus in some of the cases by hysterography with the aid of a balloon introduced into the uterus eight days after birth had taken place. In all the other cases we took extra-abdominal measurements of the contractions by means of a somewhat modified Dodek's tokometer. We combined these two methods

of examination in two cases, using them both simultaneously. They gave exactly the same results.

The persons submitted to hysterographical measurements were women in confinement, from 18 to 37 years of age, most of whom were primiparae, though there were some among them who had given birth to children two or three times, and one seven times.

The time at which the experiments were carried out varies greatly, from one hour to eight days post-partum. The majority were performed on the second to the fourth day of confinement.

Hysterography was performed on 29 persons in all. Of these 29, eight had been given fluid extract of ergot (*extractum fluidum secalis cornutum*) (Ph. Dan.) as we thought it would also be of value to draw a comparison between the action of therapeutic doses of ergometrine and that of therapeutic doses of fluid extract of ergot, as the preparation of ergot most used in Denmark.

Table I gives a summary of the classification of the persons experimented on.

TABLE I.

Classification of subjects of experiment.

Ergometrine		Fluid extract of ergot (Ph. Dan.)	
By the mouth	8 persons	By the mouth	4 persons
Intramuscularly	8 ,,	Intramuscularly	4 ,,
Intravenously	3 ,,		
Rectally	2 ,,		
Total	21 persons	Total	8 persons

Tables II, III and IV show the effect on the uterus.

In Table II it is seen that two of the women received only 0.1 mg. of ergometrine. These two are, therefore, excluded from the general appreciation which, for our purpose, only concerns the effect of therapeutic doses.

It furthermore appears from Table II that 0.5 mg. of ergometrine administered by mouth acts rather more quickly than 50 drops of fluid extract of ergot, and it would seem that the effect of ergometrine lasts longer than that of the extract. (See Figs. 2 and 3).

TABLE II.

Effect of ergometrine and fluid extract of ergot (Ph. Dan.) given by the mouth.

	From administration to commencement of effect (minutes)	Duration of effect (minutes)
Ergometrine, 0.5 mg.:		
No. B716/35	13	over 60
No. B755/35	14	,, 45
No. B755/35	7	,, 75
No. B785/35	5	,, 360
No. B786/35	9	,, 110
No. B795/35	9	,, 120
Ergometrine, 0.1 mg.:		
No. B894/35	20	,, 30
No. B944/35	13	,, 32
Fluid extract of ergot, 50 drops:		
No. B755/35	11	70
No. B786/35	18	over 60
No. B763/35	14	15
No. B795/35	10	over 120

TABLE III.

Effect of intramuscular injection of ergometrine and fluid extract (Ph. Dan.).

	From administration to commencement of effect (minutes)	Duration of effect (minutes)
Ergometrine, 0.25 mg.:		
No. B1064/35	1	over 48
No. B1093/35	6	,, 45
No. B1091/35	3	,, 45
No. B1116/35	5	,, 60
No. B1144/35	4	,, 60
No. B1146/35	7	,, 40
No. B1147/35	7	,, 33
No. B1146/35	7	,, 42
Fluid extract of ergot, 1 c.c.:		
No. B1064/35	18	20
No. B1147/35	18	10
No. B1144/35	40	over 25
No. B1116/35	No effect	

Table III shows the effect of intramuscular injection of ergometrine and of fluid extract of ergot. This table clearly shows that 0.25 mg. of ergometrine, administered intramuscularly, acts far more quickly than 1 c.c. of fluid extract of ergot, and that the effect lasts longer. (See Figs. 4 and 5).

TABLE IV.

Effect of intravenous and rectal injection of ergometrine.

	From administration to commencement of effect (minutes)	Duration of effect (minutes)
Ergometrine, 0.1 mg. (intravenously):		
No. B915/35	1	over 17
No. B914/35	1/10	,, 57
No. B937/35	1	,, 38
Ergometrine, 0.5 mg. (rectally):		
No. B1252/35	6	,, 25
No. B1261/35	8	,, 30

The effect of ergometrine when administered intravenously, and rectally (respectively 0.1 mg. and 0.5 mg.) is seen in Table IV.

It is evident that the effect of intravenous injection appears very quickly (see Fig. 6). The last two experiments show that the desired effect appears very quickly also with rectal injection.

Over and above the experiments we have mentioned here, we have used ergometrine in 75 cases of post-partum haemorrhage.

Table V is a summary of the dosage of ergometrine in the cases of these patients.

We also used this material to ascertain the amount of haemorrhage. The loss of blood was less than 500 gm. in 57 patients, between 500 and 1,000 gm. in 15, one lost 1,100 gm., one 1,300 gm., and one 1,900 gm. The three last patients were among those given intravenous injections of ergometrine. There was no accumulation of blood in the cases of any of the patients after the first administration of ergometrine, and those who were given one tablet (0.5 mg.) an hour later suffered such slight loss of blood that it could not be measured. The result of the treatment with ergometrine has thus been satisfactory in every single case.

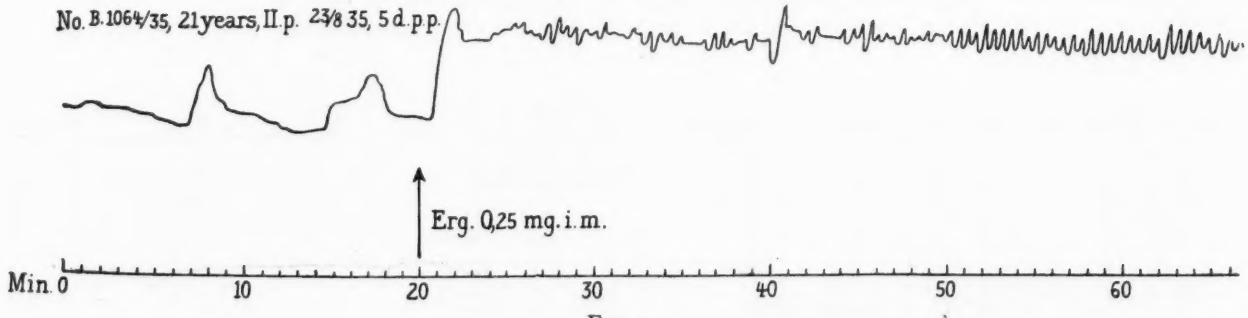

FIG. 5.

Tracing made the fifth day post-partum with the external apparatus. 0.25 mg. ergometrine (Dan.) is given intramuscularly. Effect about one minute later.

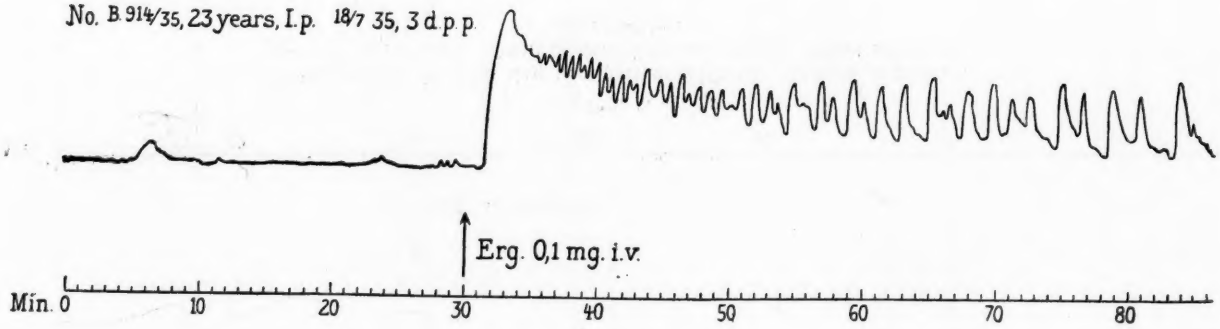

FIG. 6.

Tracing made the third day post-partum by the extra-abdominal method. Intravenous injection of 0.1 mg. ergometrine (Dan.). Effect one minute later.

TABLE V.

Summary of 75 patients to whom ergometrine was administered for post-partum haemorrhage.

Patients	Ergometrine administered
42	1 tablet = 0.5 mg.
4	2 tablets of 0.5 mg. at an interval of 1 hour.
9	0.25 mg. intramuscularly.
11	0.25 mg. intramuscularly + 1 tablet (0.50 mg.) 1 hour later.
4	0.1 mg. intravenously.
1	0.1 mg. intravenously + 1 tablet (0.50 mg.) 1 hour later.
4	0.1 mg. intravenously + 0.25 mg. intramuscularly (simultaneously).

To the ultimate question whether anything essentially new, or more advantageous, is obtained by the use of ergometrine in obstetric practice, the answer is:

In cases of slight haemorrhage, when the doctor or midwife is of the opinion that 50 drops of fluid extract of ergot (one or more times) will produce sufficient effect, there is no especial reason to employ ergometrine, although it acts more quickly and its effect is of longer duration than that of the extract.

But when the haemorrhage is greater, and possibly dangerous, and it is a question of obtaining a rapid and potent effect, intramuscular or intravenous injection of ergometrine is advantageous. We are of the opinion that ergometrine thus administered is superior to the preparations of ergot known hitherto.

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Two Rare Cases of Inversion of the Uterus.

BY

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THE two cases reported are rare and, therefore, of interest. The first shows a combination of puerperal and tumour inversion, while the other exhibits a pathologically complete inversion with partial inversion of the vagina.

CASE 1. This patient had her first confinement at the age of 21 years, in 1920. I saw her in 1925, on account of one-child sterility. Examination of the pelvis, with dilatation and curettage, did not reveal anything of note; the uterine cavity measured three inches. Menstruation was regular, with a moderately free flow. In 1927 the patient became pregnant for the second time; pregnancy and labour were uneventful. The third stage was prolonged to two hours, but the placenta finally came away by expression. Clots were passed in the first few days. Involution was slow, but the ultimate recovery was good. I saw her again in 1930, because she thought she might be pregnant, as there was a feeling of fullness in the lower abdomen. The periods were now more profuse, with clotting, but still regular. The uterus was just palpable above the symphysis pubis, and it was found to be about the size of a three months' pregnancy, and the fundus had an irregular outline. An interstitial fibroid was diagnosed, but she was unwilling to undergo operation. She was treated by deep X-ray therapy, and the loss at the periods became less, but the uterus was not reduced in size.

In 1934, as a result of increasing menorrhagia, she consented to operation, and, as the haemoglobin was only 60 per cent, she was given iron to improve the anaemia, and almost immediately became pregnant. Pregnancy was again uneventful, labour was precipitate, and the placenta was expelled in 20 minutes. There was not any unusual haemorrhage, and the uterus was firm, but above the level of the umbilicus. Progress during the first week was good, except that the lochia were profuse, and the uterus still remained at a high level. On the ninth day she complained of abdominal pain; the uterus was tender, and the temperature rose to 101°F. These symptoms continued intermittently for the next two weeks, and by the end of the fourth week, all symptoms had abated; but the uterus was still only two inches below the umbilicus. On the thirtieth day of the puerperium she was awakened with severe bearing-down pains, which she described as, "exactly as if she were having another baby." The pains lasted three hours, then ceased, and she had complete relief. When I saw her on the following

day, the abdomen was found to be flat, and the uterus could no longer be felt by palpation. There was a penetrating putrid odour in the room. Vaginal examination revealed a large soft tumour lying inside the orifice, and its attachment was readily traced to the fundus of the uterus, which was partially inverted. At a higher level the cervix formed a ring through which the inverted uterus could be felt to pass. She was anaesthetized, and a degenerating mass of a greyish colour, almost as large as a grape-fruit, but flattened, with a broad sessile attachment to the inverted fundus was removed by the fingers. Small fragments of the tumour were left, but attempt was not made to enucleate them from the uterine wall. Reduction of the inversion was then carried out without difficulty or haemorrhage. The uterus was packed with gauze soaked in flavine and glycerine, which was removed in 48 hours. There was a slight rise in temperature for two days, but never above 100°F., and otherwise her recovery was uninterrupted. On examination a fortnight later, the os admitted a finger-tip only, the uterus was but slightly enlarged, and all discharge had stopped. She is now, one year later, perfectly well with normal periods. The tumour was a simple fibro-myoma, showing extensive mucoid and hyaline degeneration.

Case 2. The second case was an unmarried nullipara of 44 years of age, who had been an inmate of a mental institution for 15 years. There was a history of menorrhagia for over one year, and she was becoming gravely anaemic. There was not any pain until one evening when she complained of abdominal discomfort, and indicated the vagina as being the chief seat of the trouble. She passed a disturbed night, and there was flooding. In the morning a discoloured mass was seen protruding from the vagina. There was not any history of severe shock, her pulse-rate was in the region of 110, and the pain had vanished. I saw her the following day, and a tumour considerably larger than a closed adult fist was lying on the perineum. Closer inspection revealed that the tumour consisted of two parts, a distal portion of a bluish-red colour, the size of a tangerine orange, and a proximal part, which showed intense pallor, and there was a definite line of demarcation between the two about the middle of the tumour, which suggested that although there was not a definite pedicle, the distal part was on the point of becoming pedunculated. The finger could be passed only about one inch into the vagina, and rectal examination showed the absence of the uterus from its normal position. Complete inversion of the uterus due to a tumour was diagnosed. The capsule of the tumour was incised and stripped, and as there was no tumour tissue embedded in the uterine wall, enucleation was easy; the raw surface was closed with mattress sutures, care being taken to avoid tension on the tissues. The remaining mass now showed the typical pyriform shape of an inverted uterus, and a ring, three quarters of an inch external to the vulva, indicated the position of the cervix. The inverted uterus was first replaced into the vagina, and then gentle pressure applied, and the fundus slipped fairly easily back into position. The uterus was found to be enlarged to 3½ inches, the walls were not unduly thickened, but rather flabby. A uterine pack was inserted, and removed in 24 hours; recovery was rapid and satisfactory. Two months afterwards she was very well and had had one period lasting three days; there was not any prolapse of the vaginal walls. The tumour was a simple fibro-myoma.

The incidence of significant fibroid tumours in pregnancy is from one (Walsh[1]) to one and a half per cent (Spencer[2]). Not only may the fibroids be a source of anxiety during pregnancy and labour, but they may still be a danger to life in the puerperium. In a pregnant woman who has a fibroid tumour, three problems have to be dealt with, one being the effect of the fibroid on the puerperium.

Cameron[3] includes in a list of complications of fibroids in the puerperium, post-partum haemorrhage, retention of the placenta, and local or general sepsis if the tumour has been bruised during labour. He also mentions expulsion of fragments of the tumour with the lochia, which, in his opinion, accounts for the occasional disappearance of a fibromyoma after labour. Red degeneration, liquefaction, and absorption have also been suggested as possible explanations of the disappearance of moderate-sized fibroids after labour. (Watson[4]).

De Lee[5] refers to troublesome haemorrhage during the third stage, particularly if the placenta is situated wholly or partly on the tumour. Adherent placenta and the persistence of profuse lochia with clots, and severe after-pains are also encountered. On the other hand, in Watson's series of 157 cases, adherent placenta is reported only twice, and post-partum haemorrhage in three cases, and in none of them was it severe. (Watson[6]).

Infection of a fibroid in the puerperium occurs either as a result of bruising during delivery, or consequent on degenerative changes during pregnancy, which render the tumour more liable to be infected by putrefactive organisms. Lockyer[7] refers to the liability to infection of submucous fibroids, and reports one such tumour which sloughed in the puerperium, and came away without operation.

Expulsion into the vagina, especially of the submucous pedunculated variety, is a relatively frequent event.

Tumour inversion has but rarely any connexion with the puerperal state, since the presence of the type of tumour most likely to produce inversion is unfavourable to the occurrence of pregnancy (Swayne[8]). Spencer[9] reports two cases of tumour inversion following abortion and labour, and he and Lockyer[10] each report a case of inversion accidentally produced in an attempt to perform vaginal myomectomy.

Gemmell[11] describes a case of a sloughing fibroid tumour causing partial inversion of a puerperal uterus, accompanied by gangrenous changes in the posterior uterine wall. Vaginal

myomectomy was performed, but as a tear was found in the posterior uterine wall supra-vaginal hysterectomy was then performed. The patient recovered after a stormy convalescence.

Treatment. Complete agreement is wanting as to the best method of dealing with fibroids complicating the puerperium. Spencer recommends vaginal myomectomy as the best treatment for submucous fibroids, even when they are infected or invert the uterus. This treatment he successfully carried out in all three cases already referred to. He advocates that it should be tried before resorting to hysterectomy, which he has never found to be necessary. Lockyer's case, in which he inadvertently produced partial inversion, in attempting to remove a fibroid, was successfully treated by vaginal hysterectomy.

De Lee advises that sloughing pedunculated tumours should be removed *per vaginam*, but not too early, unless there is severe bleeding. He believes in expectancy at first in the presence of infected tumours, until the immunities of the patient are developed. Polak[12] believes that intra-mural growths particularly may diminish in size and disappear during involution, but favours early radical operation if necrosis or infection of the tumour should create an emergency. Fischmann[13] advises that conservatism should be practised as long as possible. Reports from other sources record a stormy convalescence but ultimate recovery, following subtotal hysterectomy for a submucous fibroid in the puerperium (Lepage and Vaudescal[14]), an uneventful recovery when a submucous fibroid was removed by digital dissection (Gonnet[15]) and a successful result with a vaginal myomectomy (Mann and Lowenburgh[16]).

Inversion of the uterus by a tumour occurs in 13 per cent of cases (McCullagh[17]). It is commonest in association with submucous or pedunculated fibroids, which account for 95 per cent of tumour inversions, the remaining 5 per cent being due to a sarcoma, adenocarcinoma, or an endothelioma (McCullagh[18]). The pathological form of inversion is rarely complete, but Lockyer[19] depicts a case in which a submucous fibroid had dragged the whole vagina outside the vulva. Reports of cases of complete inversion due to tumour are not frequent, and one is recorded in a nullipara as being an unusual occurrence (Johnstone[20]), and also because of the easy way in which the tumour was reduced. In this particular case the tumour was not removed prior to reduction owing to circumstances, and at the time of the report the tumour was still *in situ*. Another was reported because of its rarity (Branch[21]), and was treated

by removal of both tumour and uterus, as it was considered inadvisable to replace a uterus which had probably been inverted for seven years. Spencer[22] and M. Rawlins[23] report cases of inversion of the uterus due to fibroid tumours, which were treated by myomectomy followed by immediate replacement of the uterus.

A very thorough examination is necessary before any definite diagnosis is made, or operative procedure decided upon, as cases have been previously recorded in which an inverted uterus, or part of one, was removed, under the impression that the tumour was a pedunculated submucous fibroid.

The removal of a tumour in an inverted uterus requires great care, as, in a series (Swayne[24]) of 83 collected cases, the uterus was torn in 12, and the peritoneum opened, during the operation of vaginal myomectomy. Such an accident may lead to general peritonitis. To avoid this, the capsule should first be opened, and the tumour enucleated. In pathological inversion the tumour should be removed first, followed by replacement of the uterus. Reduction is often comparatively easy, as I found in my own case, because the inversion was of a short duration, and changes resulting from circulatory interference over a long period had not had time to produce any pathological effects. The question as to the relative merits of an Aveling's repositor versus an operation did not arise.

Conclusions.

1. Tumour inversion in the puerperium is an exceedingly rare occurrence.

2. There is not complete general agreement as to the treatment. In the case now reported conservatism gave good results, and should a future occasion arise, I should be again disposed to follow De Lee's dictum, and "trust Nature a little."

3. Tumour inversion apart from the puerperium, accounts for 13 per cent of cases, and by far the larger majority are due to fibroids, sessile or pedunculated, growing from the fundus.

4. Complete pathological inversion is less common than the incomplete variety.

5. Vaginal myomectomy, first incising the capsule, then enucleating the tumour, followed by immediate replacement of the uterus would appear to be the ideal treatment in all cases in which access to the growth is possible. In many cases the uterus is easily replaced.

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24. Swayne (quoting Thorn). "New System of Gynaecology" (Eden and Lockyer), ii, 701.

Roentgen Pelvimetry.

BY

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(Dir. Prof., Dr. J. van Ebbenhorst Tenbergen).

IN 1922 Dr. J. V. Ebbenhorst Tengbergen, at that time charged with the Roentgenological work in the University's gynaecological clinic of Prof. Van Rooy in Amsterdam, described a method of Roentgen-pelvimetry, by which the exact size and form of the whole pelvic inlet could be measured. Briefly this method is as follows:

The measuring of the true conjugate is comparatively simple, as is shown by Fig. 1. This figure represents the median plane of a patient lying on her back on the table. P is promontory, S is symphysis, P–S is the true conjugate. When the focal spot of the tube T_1 is put perpendicularly above a point L, lying in the median plane, then the focal spot is also within this same plane. In making an exposure, P will appear on the film as P_1, and S as S_1. When a second exposure is made after shifting the tube in the median plane parallel to the film (T_2) then the points P_2 and S_2 are obtained on the film. As may be seen from the drawing, inversely the true conjugate can be constructed from the film obtained, if the height of the focal spot above the film (T_1–L) and the shifting of the tube (T_1–T_2) are known. For this one need only measure the distances from the points P_1, P_2, S_1 and S_2 to L (indicated by the shadow of a plumb-bubble which has lain on the film, and draw these in the correct relation on paper. Next LT_1 is drawn perpendicular to L, T_1T_2, perpendicular to T_1L, and then T_1P_1, T_1S_1, T_2P_2 and T_2S_2. The points of intersection of the latter lines are the extreme points of the true conjugate.

In order to measure the whole pelvic inlet Dr. van Ebbenhorst Tengbergen took for granted that all the points of the pelvic inlet are lying in one flat plane. In reality the pelvic inlet plane is not a flat plane, but the error committed in taking this for granted is very slight. When the patient is lying as symmetrically as possible on the table, i.e. in such a way that corresponding bilateral points of the pelvic inlet are on the same height above the film, then the plane of the pelvic inlet is nearly always perpendicular to the

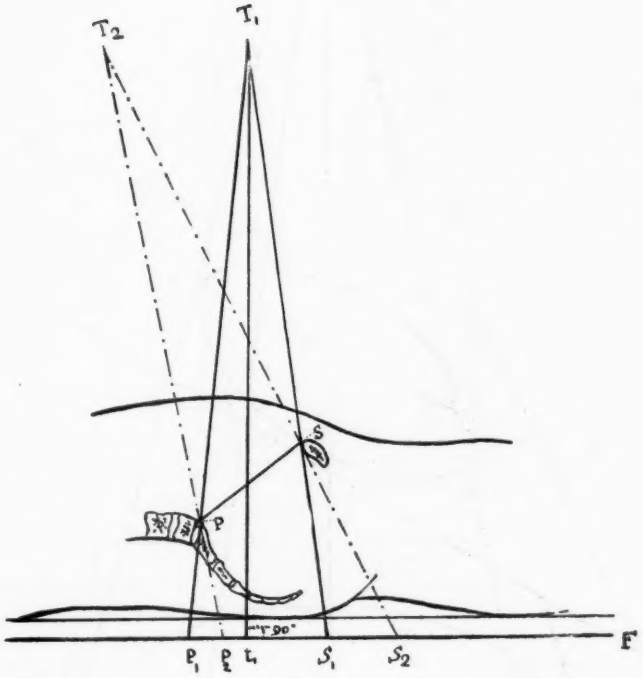

FIG. 1.

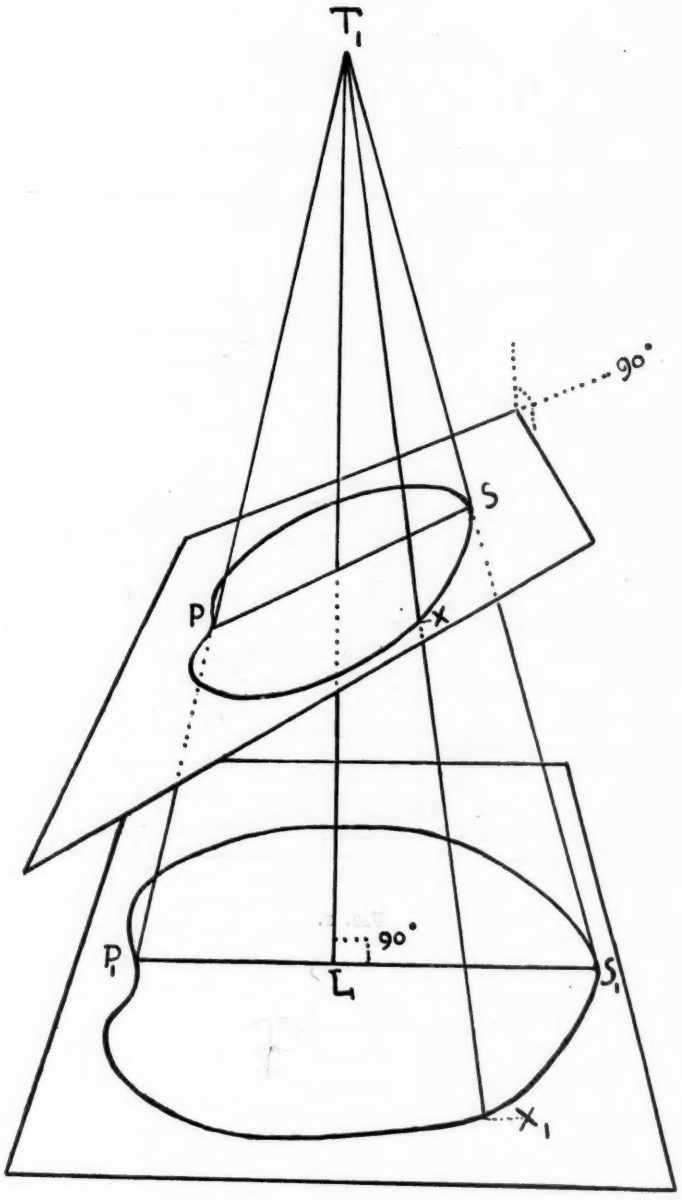

FIG. 2.

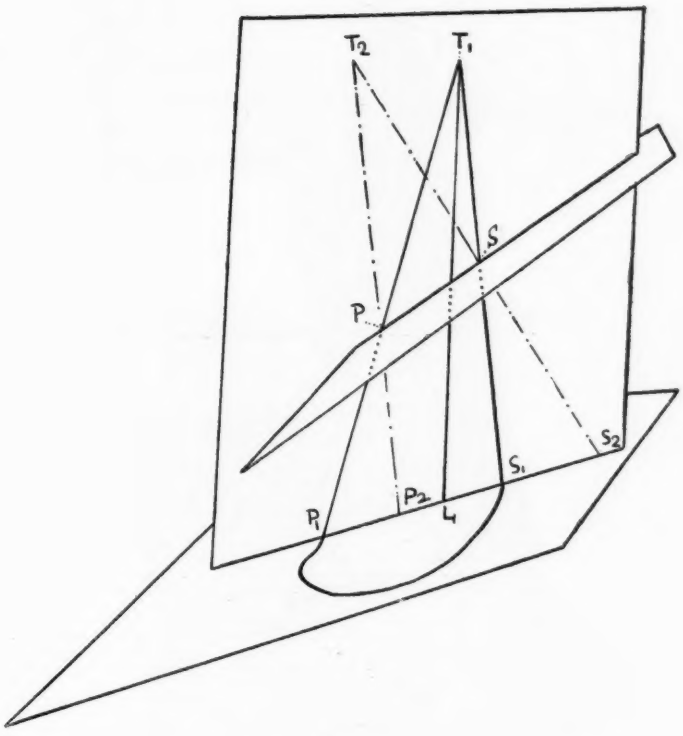

FIG. 3.

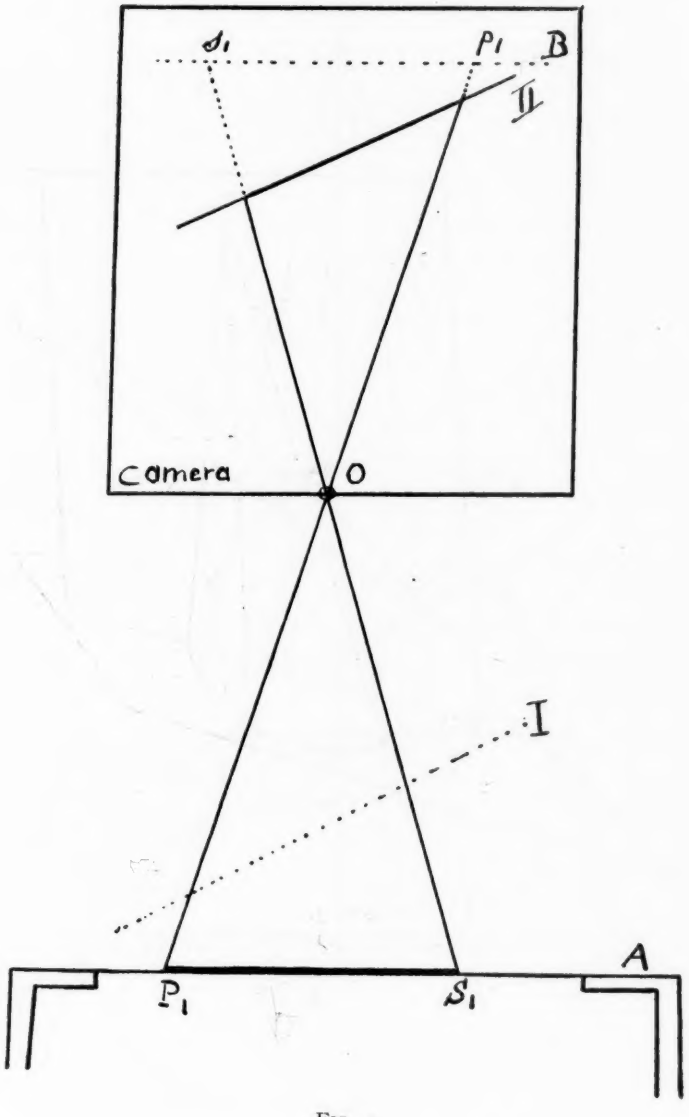

FIG. 4.

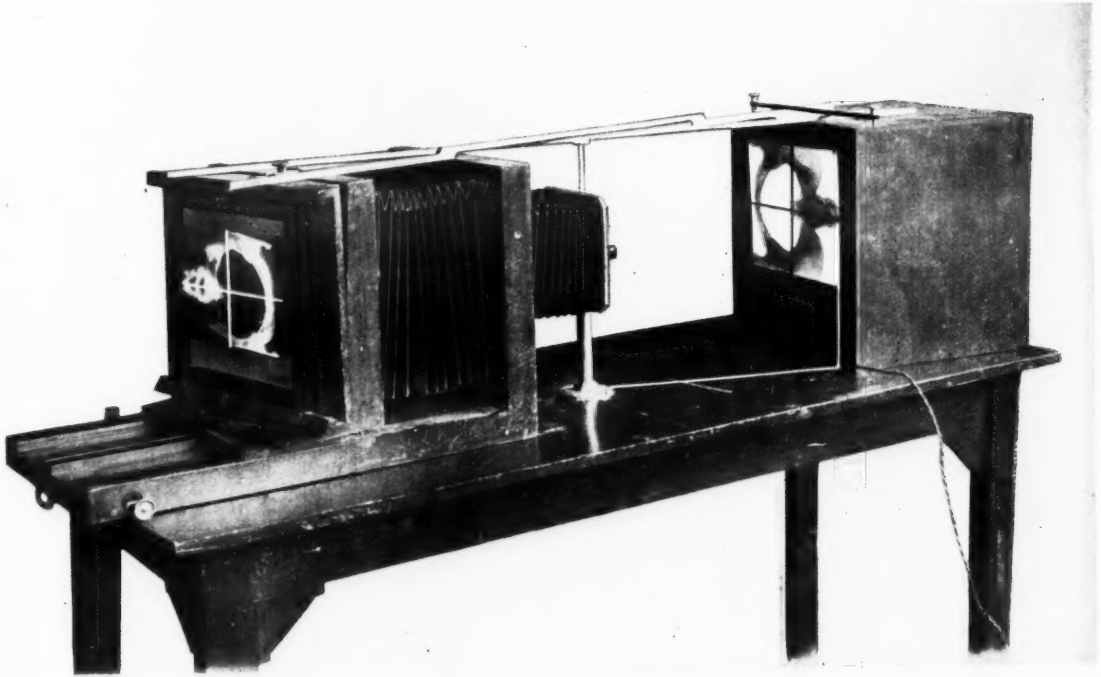

FIG. 5.
Redressing apparatus.

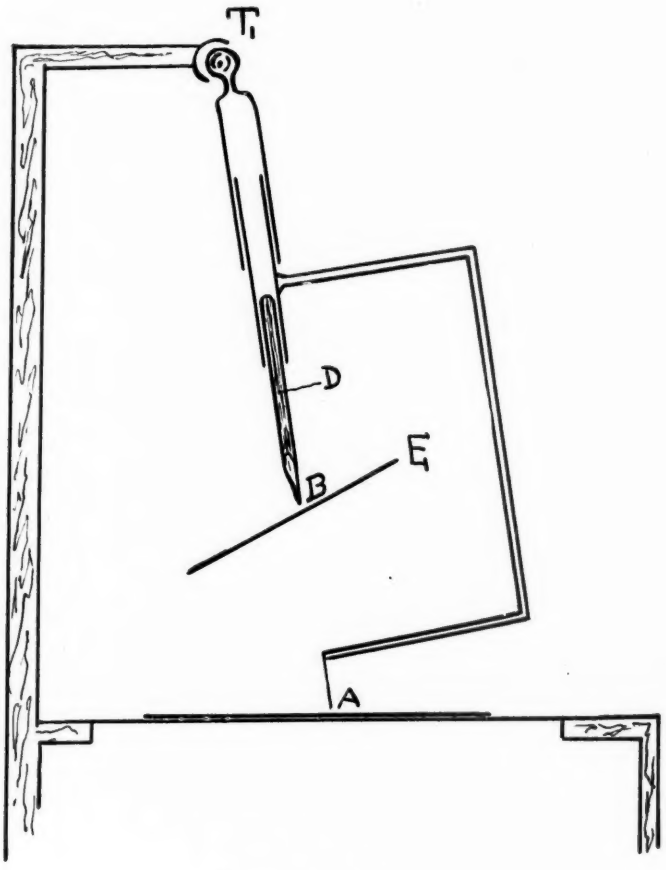

FIG. 6.

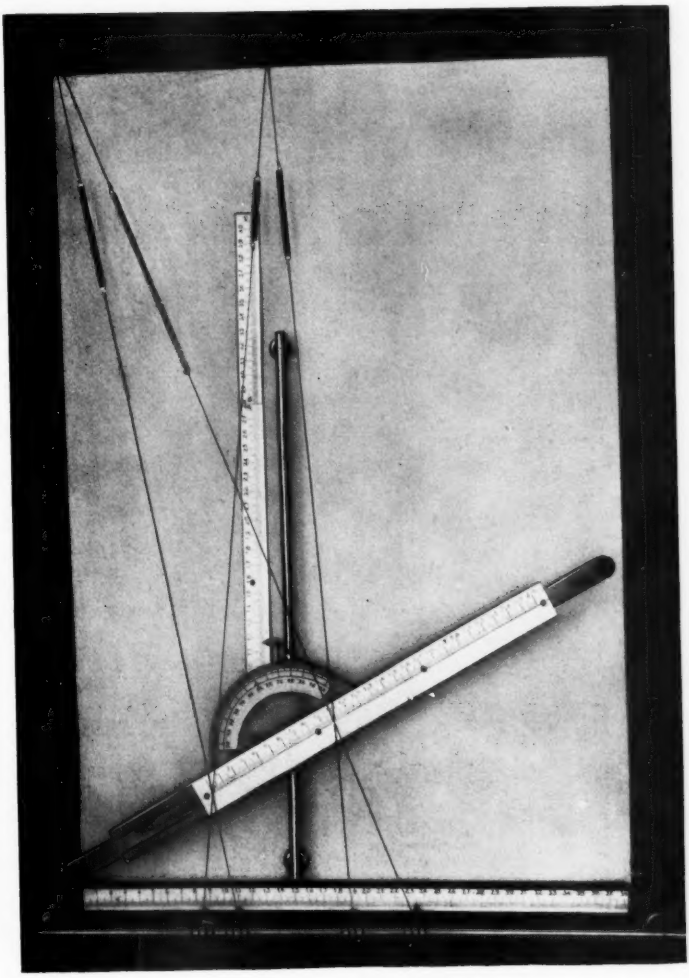

FIG. 7.

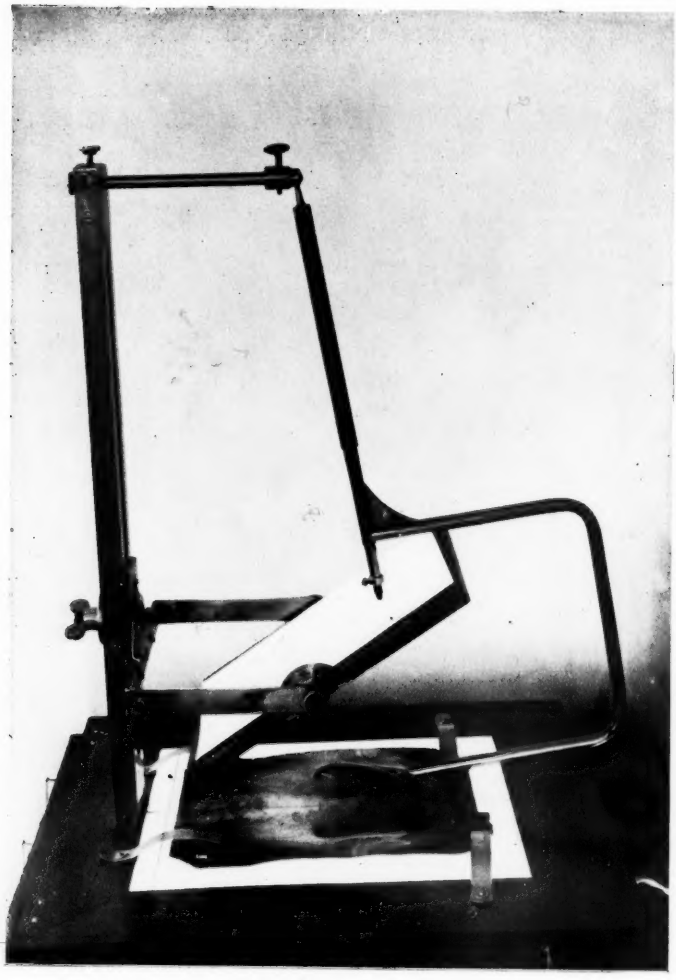

FIG. 8.

median plane. In Fig. 2 this pelvic inlet plane is drawn as well as the film with an image of the pelvic inlet as obtained by the first exposure (T_1 perpendicularly above L). The straight lines starting from T_1 represent the X-rays. Just as in Fig. 1, P_1 is the image of P and S_1 of S. Another point (X) of the pelvic inlet is represented in X_1. It is apparent that every point of the pelvic inlet and its image on the film must lie in a straight line with T_1. Reversing the process, if a point T_1 and the film are placed in respect to each other exactly as during the first exposure, and a plane is put in the same place where the pelvic inlet plane of the patient was during the exposure, then the way of the X-rays may be reconstructed. For that purpose every point of the pelvic inlet figure of the film is connected by a straight line with T_1, the points of intersection of these lines with the pelvic inlet plane forming a figure representing the true pelvic inlet of the patient. In other words, the pelvic inlet of the film is "redressed" to the true form of the pelvic inlet.

To obtain this result, two things must be done. In the first place one must know how the plane of the pelvic inlet of the patient has been placed during the exposure. This may be constructed as in Fig. 1. It is possible, e.g. to carry out the construction on a piece of cardboard as described above; when a cut is made in the cardboard according to P–S and through this a second piece of cardboard is pushed perpendicularly to the first, then a reconstruction of the pelvic inlet plane is obtained (see Fig. 3). In putting the first piece of cardboard perpendicular to the film in such a way that P_1 and S_1 come on the equivalent spot of the film, then a reconstruction of the situation during the exposure is obtained.

The second thing which one ought to be able to do is to draw straight lines from T_1 to the pelvic inlet figure of the film for "redression." It goes without saying that this is impossible in this case, as the second cardboard is in the way. Dr. van Ebbenhorst Tengbergen now devised a method of redressing rendering this possible, an optical method. When in Fig. 3 the second cardboard is substituted by a glass plate and the film is put on an illuminating box, then the redressment may be performed as follows: You keep one eye exactly on point T_1 and look at the film. When you now move a black point over the surface of the glass plate, then every time a point of the film will become invisible. The invisible spot of the film, the black point on the glass plate and the eye always lie in a straight line. When you note down on the glass plate the place of the black point every time

when a point of the pelvic inlet figure of the film becomes invisible, then you get on the glass plate an image representing the real pelvic inlet. The dots noted on the glass are obviously nothing else but the point of intersection of the straight lines connecting T_1 with the pelvic inlet figure of the film with the pelvic inlet plane.

The same result may be obtained by means of photography (see Fig. 4). C is a large camera, the opening O of which is put exactly on T_1. The film A is again fastened to an illuminating box. On a photographic plate B put in the camera on the same distance from O as the film, the same picture of the pelvic inlet is obtained as on film A. You will notice that this picture is formed by rays radiating from O and taking the same way as the X-rays during the exposure. When you thus put a photographic plate II in the same position to B as plane I (the pelvic inlet plane) is with respect to A, then you get on plate II a redressed photograph of the pelvic inlet. Fig. 5 shows the apparatus as it is used in practice.

The author now devised another redressing method, to wit, a mechanical one. Fig. 6 shows the principles thereof. On point T_1 a ball-and-socket joint is fitted in which a bow can turn. The bow can be moved upwards and downwards, so that the lowest point A can be placed on every part of the film. The staff D can also be moved up and down and contains on point B a pencil. As may be seen T_1, B and A always lie in a straight line. When the film and plane E (which may be a wooden board) are put in the correct position in relation to T_1 and we follow with point A the pelvic inlet figure on the film, then B draws on plane E the redressed pelvic inlet figure.

The practical execution of a measurement of the pelvic inlet is carried out in the following manner: The patient is lying on her back on the Potter Bucky diaphragm, as symmetrically as possible. On the centre of the film is laid a plumb-bubble or a plumb-cross. The focal spot of the tube is adjusted exactly 60 cm. perpendicular to this. Then the first exposure is made. After this the tube is shifted exactly 15 cm. in the direction of the patient's head, and the second exposure is made. In the meantime the patient must remain motionless. It is preferable that the two exposures are not made on one film, but on two. The pictures then become sharper, and for the measuring it is immaterial whether one or two films are used, provided that care is taken that the plumb-bubble is lying during the second exposure on the same place. At the second exposure it is advisable to tilt the tube

in such a way that the central ray passes the centre of the pelvic inlet. Care should be taken, however, to keep the focal spot of the tube always 60 cm. above the film. On the pictures obtained the distances from the upper edge of the symphysis to the plumb-bubble are measured. The promontory is not always clearly visible; for this reason we take the upper edges of the superior straits which are always clearly defined and are also lying within the pelvic inlet plane. We draw a line touching these two curves and we determine the point of intersection of this tangent with the median line. The distance from this point of intersection to the plumb-bubble is measured. In this way we obtain all the data we need. We begin by constructing the correct position of the pelvic inlet plane. For this purpose a construction-table is made (Fig. 7). As we see, this is entirely identical with Fig. 1. At the bottom there is a bar on which rings can slide. Every ring is connected by a cord ending in a spring with one of the two points at the other side which are at the distance of 60 cm. from the bar. Above the bar there is a graduated scale by which the rings may be put in the correct place. On the place of T_1–L there is a second bar on which a ring can slide. On this ring a lath is affixed in such a way as to render it possible for the lath to turn in the middle of the ring. By sliding and turning, the lath is adjusted in such a manner as to pass through the points of intersection of the cords, representing P and S. You can read from the graduated arc the angle formed by PS and the vertical bar, and on a graduated scale the height of the point of intersection of PS with this bar.

The redressing apparatus is represented in Fig. 8. When Fig. 2 and Fig. 6 are again examined, the construction will be clear. The horizontal bar to which the ball-and-socket joint is attached can be slid through the vertical bar, so that the ball-and-socket joint can be adjusted in the place of T_2. In this case the second picture ought to be used for the redression (this is even advisable, as details on this picture are often better). The film is now laid in the right place on the illuminating box and fastened with clips. On the illuminating box a line is drawn on which the median line will be placed, and the point on which the image of the plumb-bubble or plumb-cross will come. Hereafter the little board is adjusted to the right height; the graduated scale of the vertical bar is similar to the vertical graduation scale of the construction table. Next, the board is moved till it forms the right angle with the vertical. On the board a sheet of paper is affixed, and then the redression is executed in the manner described above.

Conservative Therapeusis in Gynaecology.

BY

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INTRODUCTION.

DURING the latter half of last century, gynaecology underwent a rapid and progressive evolution. The modern conception of endocrinology, which now takes a leading place in the medical progress, and which might have been delayed for a century or more without the penetrating researches of Claude Bernard and his stimulating influence upon his pupil, Brown-Sequard, has given the science and art of gynaecology a greater impulse during the last decade.

Recent disclosures have added greatly to the understanding of gynaecological physiology and have virtually revolutionized gynaecological therapy. The gynaecologist is fast changing his views of radicalism into conservatism, but he often hesitates, when faced with the two difficult problems, i.e. (1) the chance of recurrence of the disease, and (2) the subsequent results of castration, or of depriving a young woman of the physiological function of her sexual organs. The solution of these problems is his constant worry at the operation table. If he decides upon a conservative operation, the recurrence of the disease and the possibility of a second operation is often his nightmare. On the other hand, he finds in the out-patient department of his hospital several of these poor victims of radical operations, who daily cry, without relief, to the gynaecologist about their multifarious aches, pains, and sensations, and many a time insist that they are worse than they were before the operation.

How, then, can we reconcile the two? Are the conservative operations successful or justifiable? Is it worth our while to take

a chance and perform a conservative operation, at the risk of recurrence of the disease or a subsequent operation, to save the patient from the effects that may follow a radical operation.

Unfortunately, there are differences of opinion among the gynaecologists on these points. The intensity or degree of menopausal and other troubles which follow radical operations are still *sub judice* with some, and the precise indications for a conservative operation vary according to the point of view of the gynaecological surgeon.

A Plea for Conservative Gynaecology.

After long and continued experience, gradually acquired during the last 26 years, with the sequel of gynaecological operations, and encouraged with the results of some of my tentative conservative operations, I have learnt to be conservative whenever possible.

All conservative gynaecological surgery is centred round the safeguards of the ovary and the uterus, whose complex rôle is the physiology of the menstrual function, of the sexual life of the woman and of the menopause, is now too well known and needs no comment—*tota mulier in ovario*.

The success in conservative gynaecology, however, greatly depends on (1) the preservation of the uterus, or a greater part of it, with at least one or a healthy part of an ovary, (2) on the integrity of the circulation of the organ operated upon, and (3) on the amount of trauma caused to the organ.

Unfortunately a great number of patients seek admission to the hospital when the disease is too far advanced and when conservative treatment is not possible.

In a consecutive series of 852 laparotomies performed by me at the King Edward Memorial Hospital, Bombay, and at my private hospital, from April 1926 to May 1934 (eight years) conservative operations could be undertaken in only 328 cases. (Table I, on page 1168, shows the number and the nature of operations.).

Conservative Hysterectomy.

In recent years fundal and corporeal hysterectomies are advocated by several gynaecologists in order to preserve the utero-ovarian energy in young patients. Theoretically, the less the uterine tissue is sacrificed and the more the vessels are preserved the better should be the results; but in practice it is

difficult to find cases suitable for such operations. Inflammatory lesions of the fundus uteri ordinarily follow various types of salpingitis, and these invariably clear after salpingectomy. There is no doubt that sometimes one has to sacrifice the uterus in bad and chronic affections of the appendages, but these cases are bad enough for subtotal hysterectomy, and conservative fundal hysterectomy is out of question.

Diffuse fibromyomata of the fundus uteri or submucous fibroids and adenomyomata of the cornu of the uterus are not very common in young patients; they can most often be dealt with by myomectomy or resection.

In 126 hysterectomies I could perform fundal hysterectomy with salpingectomy only five times. In all these patients the Fallopian tubes were badly involved and there were very small fibroids in the fundus. At whatever level the fundus was amputated I attempted to preserve the uterine arteries. This was possible by clamping and tying the perforating branches. Light instruments were used to avoid crushing the tissues and the broad ligaments. All five patients were between the ages of 20 and 30 years. I lost sight of one; four reported themselves at regular intervals; only one menstruated, very scantily for a day, for six months after the operation. Not one of the four patients complained of any serious trouble of the menopause, but all were worrying themselves and myself because of their sterility.

Many gynaecologists deprecate high conservative hysterectomy because of the difficulties met with in the peritonization, and the subsequent possible complications. Abdominal pregnancies following high hysterectomies have been reported by some, but this complication or danger could be avoided by judicious excision of the fundus uteri. A V-shaped incision on the antero-posterior or lateral walls of the uterus will allow a better approximation and coaptation of the incised surface and closure of the uterine cavity. The peritonization in some cases is possible by utilizing the round ligaments or the broad ligaments which can be carefully preserved.

Salpingostomy.

One hundred and thirty-five conservative operations on the Fallopian tubes were performed in my series. These were unilateral, with excision of the Fallopian tube and ovary on the opposite side, bilateral with or without resection of one or both ovaries, and with or without Gilliam's suspension of the uterus. A hystero-salpingography was performed in every case of sus-

pected blockage of the Fallopian tube before the operation. Various techniques were adopted according to the site of obstruction. Wherever the adhesions were dense and the appendages were liberated from the pouch of Douglas the results were disappointing.

I am not, unfortunately, in a position to give any percentage of successes in this set of cases. Wherever the adhesions were dense and the resection of ovaries was required, the results were satisfactory. Several of these cases were subsequently subjected to hystero-salpingography. In spite of repeated questionnaires sent to the patients only 63 responded, and of these only 18 have reported to have conceived subsequently. Table II gives the results of the operation. I have confined six patients in my hospital. One patient, however, merits mention. She had three children, and was admitted for chronic retroflexion, cystic ovaries, and menorrhagia. The right Fallopian tube and ovary had to be sacrificed, and on the left side I attempted to resect the ovary and perform a salpingostomy, but at the end of the resection very little ovarian tissue was left; it was just sufficient to close the edges of the incision in the ovary. In fact, I wondered if any ovarian tissue was left. The left Fallopian tube was blocked at its distal end and salpingostomy was performed. After Gilliam's suspension the abdomen was closed. The patient had a normal labour a year after. She has had three children since the operation, one boy and two girls. She has menstruated regularly, but the menstruation has been scanty. I do not suppose that she has an accessory ovary.

Resection of the Fallopian Tubes and Implantation.

This operation was undertaken only five times for inflammatory occlusion in the uterine portion of the Fallopian tube. The results, however, were disappointing.

Resection of the Ovaries.

Resection of the ovaries was undertaken in 91 patients with or without Gilliam's suspension, for innocent small cysts of the ovary. The age incidence was between 22 and 35 years. Only fifty-two reported subsequently. Of these 21 had amenorrhoea two or three months after the operation, 15 oligomenorrhoea, and 16 regular and normal menstruation. Amenorrhoea followed mostly in those cases in which one ovary was removed and the other was resected. Out of 16 patients from whom both ovaries

were removed only nine had subsequent pregnancies. In one patient, aged 32 years, who had four children, the right ovary was removed for a cystoma and the left was resected. There were several small cysts in the ovary and very little ovarian tissue could be saved. She came to my private hospital for confinement after 13 months.

Ignipuncture and Acupuncture of Cysts of the Ovary.

In small cystic disease of the ovaries ignipuncture of the cysts and destruction of the cyst's wall was the principle adopted. When the cysts were only few acupuncture was preferred. The electric cautery was invariably used for ignipuncture. The results on the whole were unsatisfactory. Fifty-two patients were treated but very few were relieved of the symptoms.

Ovarian Grafting.

In 15 cases, some with severe inflammatory lesions and others with cystic disease of the ovaries, autoplastic grafts were used. Great difficulty was experienced to secure healthy ovarian tissue by macroscopic examination. In cases of inflammatory lesions the grafts were placed in the cellular tissue of the pubis, and only in five cases it was possible to place the grafts on the broad ligament. Two cases out of five conceived. One aborted at three and a half months and the other was delivered of a full-time female child 12 months after the operation. I have lost sight of this patient since her confinement. The results of the other grafts were not at all satisfactory.

For the sake of completeness it would be fair to mention the death-rate in the series of my conservative operations. I am pleased to say that it was *nil*.

Conclusions.

I have placed before you the results of my attempts at conservative gynaecological surgery. It is unfortunate that a good number of my patients could not be traced and much useful information has been lost. Bombay is a city of floating population. Moreover, patients come to the hospital from distant villages and it is difficult to trace them subsequently. Yet the small number of cases of success placed before you will, I trust, justify my attempts.

The indications for a conservative operation depend on the age, social condition, and general condition of health of the patient; on the pathological lesions present, on the willingness of the patient to take the risks of a prolonged convalescence or a recurrence, and on the stage of the disease.

Many a time it happens that the patient is the only child or a young woman, a fiancée, or recently married. Would we be justified to undertake a radical operation because it is simple and safe, or to attempt a prophylactic operation to preserve the physiological function of her genital organs?

With all the care in the investigation of a case the indications for a conservative operation can only be determined after opening the abdomen and knowing the exact extent of damage caused to the genital organs, and the success will depend on the experience of the operator, his knowledge of macroscopic pathology of the pelvis, and on the soundness of his judgment.

In spite of the modern advances in medical gynaecology—in vaccinotherapy, in physiotherapy, in curiotherapy, in heliotherapy, and in balneotherapy—conservative surgical therapy has its field, which, I trust, with better technique and better judgment of pelvic pathology, will fast expand.

TABLE I.

Nature of Operation.	Number.	Incidence.	Mortality.
Wertheim's operation	14	40-55	1
Total hysterectomy with removal of appendages	38	45-55	—
Subtotal hysterectomy with removal of an ovary	28	30-40	—
Subtotal hysterectomy with both the appendages	41	35-50	—
Fundal hysterectomy with salpingectomy	5	20-30	—
Salpingo-oöphorectomy, bilateral	65	30-45	3
Salpingo-oöphorectomy unilateral	55	18-35	—
Salpingostomy, unilateral	30	20-35	—
Salpingostomy, bilateral	45	25-30	—
Salpingostomy, with resection of one ovary	16	20-30	—
Salpingostomy with resection of one ovary and Gilliam's suspension	23	25-35	—
Gilliam's operation with unilateral salpingo-oöphorectomy	64	45-35	—
Double salpingectomy with removal of one ovary	45	20-30	—
Gilliam's operation with resection of one ovary	51	25-30	—
Gilliam's operation with resection of both ovaries	45	25-35	—
Gilliam's suspension	86	25-45	—
Resection and implantation of the Fallopian tubes	5	25-30	—
Resection of ovaries	15	25-35	—
Gilliam's suspension with ignipuncture or acupuncture of the cysts of the ovaries	52	30-40	—
Ovarian grafting	15	25-35	—
Oöphorectomy, single, for ovarian neoplasms	43	35-45	2 (one malignant)
Oöphorectomy, double, for ovarian neoplasms	21	35-55	3 (malignant)
Myomectomy	25	25-35	—
Exploratory laparotomy	25	25-55	6 (inoperable malignancy)
Total ...	852	—	15

TABLE II.

Salpingostomy.

In the 63 patients who responded to the *questionnaire*, the results were as follow:

No. of patients.	Nature of operation.	Results.	Secondary operation.
15	Salpingostomy with resection of both the ovaries.	Cystic changes, adhesions and chronic pain and micromenorrhoea.	Hysterectomy with salpingo - oöphorectomy was performed in five. The remainder refused any operative treatment.
7	Salpingostomy, resection of one ovary and salpingo-oöphorectomy on the other side.	Cystic changes in the ovary, amenorrhoea.	nil.
26	Bilateral salpingostomy with Gilliam's suspension.	Fifteen conceived subsequently.	nil.
13	Unilateral salpingostomy with removal of the Fallopian tube and ovary on the other side.	Oligomenorrhoea and chronic pain in eleven; two conceived.	nil.
2	Unilateral salpingostomy with resection of one ovary and salpingo - oöphorectomy on the opposite side.	Conceived after the operation (1).	
63	—	18 conceived.	—

Minor Degrees of Calcium Deficiency in Pregnancy in India.

BY

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THE question of diet in pregnancy is complicated by social customs, illiteracy and half education, age-long prejudice and various other factors in this country. The old grandmother or mother-in-law is a firm believer in what has been the custom from time immemorial and despises anything that is new. The half-educated would-be mother or young mother considers herself too ultra-modern to live on a conservative and nutritious diet.

Minor degrees of osteomalacia are very common in India. As a matter of fact, it is also common among the Indians living outside India. Cook[1] mentions that all degrees of osteomalacia were common among the Indians living in Uganda, whereas they were absent among the indigenous people. Green-Armytage[2] first drew attention to these conditions in this country and always stressed it in his teachings, and it is true that these cases give more trouble in labour and puerperium than the straightforward case of osteomalacia with deformed pelvis, as the latter is easy to diagnose and the doctor can quickly make up his mind regarding treatment. But not so with minor degrees of osteomalacia, as they are rather difficult to diagnose and can be easily missed unless the practitioner is on the look out for them.

ROLE OF CALCIUM IN PREGNANCY.

It may not be out of place to recapitulate very briefly the role of calcium in pregnancy.

The foetus needs calcium for the growth of its body. Normally, during pregnancy, the mother is storing calcium in larger quantities than are actually required by the foetus. Only during the last month does the foetus take up more calcium than is stored by the mother. That is why premature children are so liable to suffer from deficient calcification and softness of the

DIAGRAMMATIC REPRESENTATION OF CALCIUM STORAGE BY MOTHER AND ABSORPTION BY FOETUS IN THE LAST FEW WEEKS OF PREGNANCY.

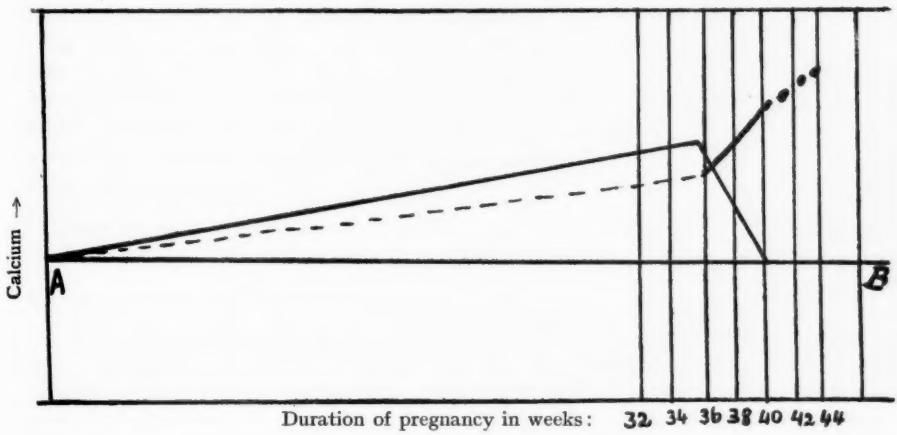

FIG. 1.

Optimal calcium level in blood—AB.
Calcium storage by mother ————
Calcium absorption by foetus - - - - - - -
Calcium absorption by foetus in last month of pregnancy ——
Calcium absorption by foetus in post-maturity .....

UNIV. OF MICH.

bones; whereas in the post-mature child, even during the space of a fortnight, the rapid calcifying process makes the skull so hard that moulding is difficult, if not impossible, and this causes difficult and prolonged labour and injury to the mother and child or even death of the child. A diagrammatic representation of calcium storage by the mother and absorption by the foetus is given in Fig. 1.

Adequacy of calcium storage depends on a sufficient supply firstly of calcium and phosphorus, and secondly of vitamin D. The latter is essential for the absorption of calcium and phosphorus from the bowel and for the normal calcification of the bones. So deficiency in any of these three will interfere with the calcium storage by the mother and its utilization by the foetus. The foetus is a parasite, and if it does not get its share it will rob the host to get its own, and consequently calcium will be depleted from the system of the mother and the latter will suffer from decalcification, the effects depending upon the degree of depletion. During lactation, too, there is an abnormally high demand for calcium.

Causes of Calcium Deficiency in India.

1. *Insufficiency of Calcium Supply.*

Milk is the only natural source of supply. Most Hindu women are vegetarians, and for them milk is the only source. In big cities it is difficult to obtain good milk at moderate prices, and very few poor people can afford it. In villages the usual custom is that several families live together, and by the time the needs of the other members of the family are met in a poor middle-class family, very little is left for the young would-be mother, and she has to do without it. The modernized young women despise milk, as it is too old-fashioned a drink.

2. *Insufficiency of Vitamin D.*

The usual sources in the ordinary diet are yolk of egg, milk and butter. The amount present in milk is very little. Fresh butter seldom forms part of the ordinary Indian diet. Eggs are usually not eaten by Hindu women. The food is generally cooked in overboiled butter (ghee) or vegetable oils. Unboiled milk is drunk only in the Punjab. In most of the other provinces overboiled milk is the usual form in which it is taken.

No doubt the vitamin is produced by the action of the sun's

rays on the skin. Although there is no dearth of sunshine in the country, it is almost unbelievable how the sun is kept out. Most women live indoors. In big cities it is not possible for the average person to have enough open space inside the house to let the sun in. In the villages of Bengal and Behar and in Bombay and Madras presidencies, the womenfolk lead a more or less open-air life. In the Punjab the conditions are totally different—houses are built one sticking to the other, and a village is a mass of houses with very little space in between and far less inside the house. The poorer class of women do not observe 'purdah' (confined indoors). The well-to-do usually have enough space inside the house for the womenfolk to sit out; some of them do not observe 'purdah.' The middle-class people can neither afford enough space inside the house nor can they easily shake off the social custom (purdah), and are, therefore, the worst sufferers.

3. *Excess of Cereal Element in the Food.*

It has been shown that when a diet has a barely minimal vitamin D content, rickets can be precipitated by increasing the amount of cereal content in the food. Mellanby[3] suggests that the cereals may contain some harmful substance which antagonizes the action of vitamin D. In the diet of all Indians, whether in or out of India, and the Chinese, the cereal content is exceedingly high, and these are the two countries where osteomalacia is most rife, and they get plenty of sunshine. This ingredient of food is also cheap, and so the hungry poor has to depend mostly on this element to appease its hunger.

The calcium and vitamin D content of the diet are no doubt at a very low level in the poorer classes, but it is not so among the well-to-do classes. Although the deficiency is far more common among the poorer classes and the manifestations are more acute, the well-to-do are not immune from it, and I have seen cases in which the symptoms of deficiency were obvious and I had every reason to believe that the supply of calcium and vitamin D were inadequate. The cereal content of the diet of all Indians, poor or rich, is very high. It is more so during pregnancy, as the proteins and fats are cut down. Therefore, the only common factor in every form of Indian diet is the excessive cereal content of the food, and this either aggravates the already low vitamin D content in most, or in some other mysterious way alters the calcium metabolism of the body and hinders its absorption and utilization.

Effects of Minor Degrees of Calcium Deficiency.

I can hardly add anything to what has already been pointed out by Maxwell[4] and Green-Armytage[5].

Dental caries is the commonest of the ailments. In some there is rarefaction of the gums, and the teeth get loose and may fall out.

All degrees of disturbances of the peripheral nervous system may manifest themselves. There may be hyperaesthesia, paraesthesia, numbness of hands and feet. Muscular spasms, e.g. cramps, spasms of the adductors, are not rare. The latter may make a vaginal examination difficult.

Muscles become flabby, and if the cardiac, abdominal or uterine muscle is affected, it may lead to other complications, e.g. tachycardia, malpresentation, and uterine inertia.

Apart from *pucca* (meaning full-blown) osteomalacia of the bones of the spine and pelvis, minor degrees of the disease are common and can be effectively treated if diagnosed early. There may be transient pains and aches in the spine, pelvis and about the costal margins. It may also lead to instability and difficulty in locomotion. But the most important factor in this group, from the obstetric point of view, is that the pubic angle may just become slightly narrowed and the pelvis funnel-shaped. This is liable to give trouble during labour, specially in a patient with a history of a previous normal labour, when the attendant does not expect any abnormality and neglects to make a thorough examination of the pelvis. Gastro-intestinal disturbances, and in some cases transient oedema, may be produced by calcium deficiency.

Occasionally the mother may remain an invalid for a long time after a diet deficient in calcium during pregnancy, and this may lead to sterility. It is probably caused by the prolonged deficiency having some deleterious effect on the ovaries or pituitary.

In some cases excessive intra-uterine movements of the foetus are due to calcium deficiency as they cease on the administration of calcium.

Malnutrition and rickets of varying degree are often due to calcium deficiency in the maternal diet during pregnancy. It is also responsible for delayed dentition.

Conclusion.

The ordinary Indian diet must be supplemented by a liberal amount of milk, at least three pints a day. Eggs and meat need

not be forced on people who have prejudice against them, but in this case the amount of milk consumed is all the more important. If there is any suspicion, or indication of, calcium deficiency, calcium, phosphorus and vitamin D must be supplied separately.

The cereal part of the ordinary diet should be cut down as much as possible without causing real hardship (and this will always ensure adequate vitamin E supply), and the carbohydrate content replaced from other sources, e.g. potatoes, carrots, coconut, beetroot, legumes (e.g. soya bean), and sweets.

Summary.

1. The environmental conditions prevailing in the country, shortage of calcium and vitamin D in the food, and excess of cereal content in the diet are the main causes which are responsible for calcium deficiency.

2. Various ailments and complications which may be produced by minor degrees of calcium deficiency have been enumerated.

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The Effect of the Administration of Oestrone and Progesterone on the Human Uterus.

BY

M. C. WATSON, M.B. (Tor.).

OESTRONE and progesterone have been shown to have individually a definite and distinguishable role in the artificial production of changes in the endometrium which are similar to those occurring in the cyclic endometrial development of normal menstruation (Kaufmann[1], Werner and Collier[2]). These two substances have, therefore, a possible field of usefulness in the treatment of certain menstrual irregularities during the reproductive period. It occurred to us that it would be possible to make observations on the effects produced in the endometrium from the administration of these substances during the reproductive period, by carefully selecting patients for this purpose when they came to operation for other reasons.

The case reported here was considered by us to be an ideal one for this type of investigation for the following reasons:

1. The menstrual periods of the patient for the past 20 years were of a type that suggested a definite under-function of the ovaries.

2. Some further knowledge of the activities of the patient's ovaries had been obtained by examination of sections of endometrium which were recently recovered at a diagnostic dilatation and curettage which was done immediately prior to the time for the onset of menstrual bleeding.

3. The diseased condition (small submucosal fibromyomata) which caused her symptoms and made a subsequent hysterectomy necessary was one which was not likely to influence the action of the hormones to a marked degree.

4. It was possible to obtain the uterus, after hormone therapy, for the study of complete serial sections.

This patient stated that the flow at her menstrual periods had been scanty for the past 20 years. She was 36 years of age. The interval between her periods was approximately 28 days up till March 1935, when she suffered from the first attack of excessive and prolonged uterine bleeding. The interval between the onset of the haemorrhages during the succeeding months was 23 days,

and they were prolonged by one or two days over the duration of the previously normal periods. The fact that the bleeding occurred at regular 23-day intervals indicated to us that it possibly occurred after the highest point of oestrin concentration had been reached and probably in the absence of a full progestin effect from the ovaries of the patient. She was admitted to the hospital on August 16th, 1935, for diagnosis. The regular monthly bleeding had not yet occurred in August although the interval since the onset of the last attack was now 26 days. Diagnostic dilatation and curettage were performed on August 19th. The endometrium obtained at this time should represent the full hormonal effect from the ovaries as the interval since the onset of the last bleeding was 30 days at this date. Figures 1 and 2 are from sections of this endometrium. The stroma was filled with free red blood-cells showing that the onset of uterine bleeding was imminent at the time the curettage was performed.

Following the curettage the haemorrhage was reduced in daily amount, the duration was prolonged from six to eight days, and the interval between the days of onset remained approximately 23 days. The patient was kept under observation and was re-admitted to the hospital on November 17th, which was 18 days after the onset of the last menstrual bleeding. Bleeding began on November 19th and continued with a much diminished flow until November 22nd, i.e. four days' duration. One could not be certain that a large portion of the endometrium was shed during this period of uterine bleeding. It seemed probable, however, that there had not been any great increase in the activities of the ovaries of this patient since the month of August and, therefore, the endometrium obtained at that time would in a degree represent the state of development which existed prior to November 19th. Even though degeneration had not taken place prior to, or during the occurrence of, this last diminished menstrual flow, it was decided that we should be able to recognize any marked developmental differences which might be caused by the administration of hormones at this time.

The hormones were administered in the following doses, and at the times stated.

November 26th, 1935.—1 mg. (10,000 international-units) of crystalline oestrone at 2 p.m.; 1 mg. (10,000 international-units) of crystalline oestrone at 6 p.m.

November 27th, 1935.—1 mg. (10,000 international-units) of crystalline oestrone at 9 a.m.; 18.9 mg. of crystalline progesterone at 9 a.m.; 1 mg.

PLATE I.

FIG. 1. A section of the endometrium obtained on August 19th. Note the straight glands in longitudinal and cross-section. The stroma is filled with free red blood-cells. (×65).

FIG. 2. Glands in the same section as Fig. 1. Note that the cells in the epithelium are of a low columnar type with the nuclei near the centre of the cell. This represents an oestrin effect only. (×250).

PLATE II.

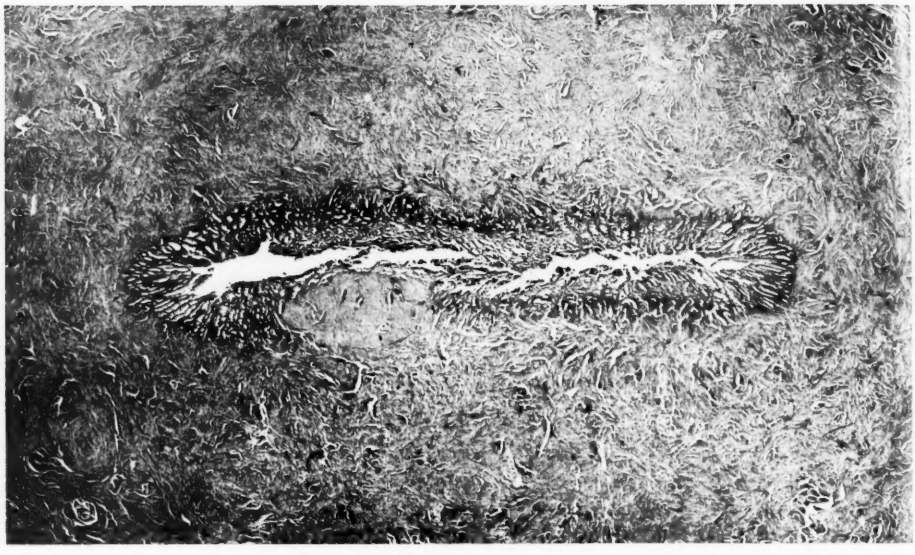

FIG. 3. A cross-section of the uterus taken near the fundus. Note the submucosal fibromyoma in section, also the premenstrual type of endometrium showing superficial degeneration. (×6).

FIG. 4. From an area in Fig. 3 at 4 o'clock. Note the coiled glands in longitudinal section. The epithelial cells show a marked secretory activity. (×65).

FIG. 5. Glands from the centre of the field in Fig. 4. Note the vacuolization in the epithelial cells with a marked increase in cytoplasm and the nuclei at the basement membrane. (×250).

PLATE IV.

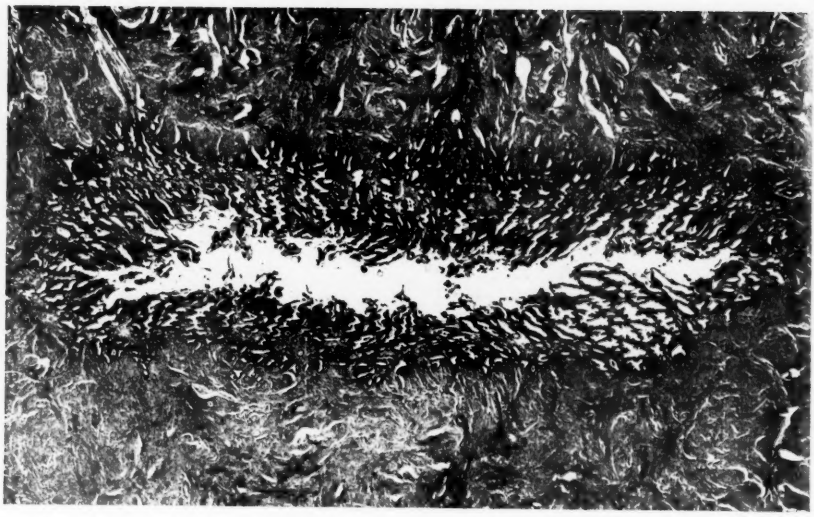

FIG. 6. A cross-section of the uterus at the mid-point between the fundus and the internal os. Note the premenstrual type of endometrium with superficial degeneration and the area showing marked glandular hypertrophy at 5 o'clock. (×12).

FIG. 7. From the area of glandular hypertrophy in Fig. 6. Note a marked hypertrophy showing free blood in the stroma and in the dilated lumen. (×65).

FIG. 8. The central glands from Fig. 7. Note the hyperplasia of the stroma and the epithelium with a marked increase of cytoplasm in the epithelial cells and the location of the nuclei at the basement membrane. (×250).

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(10,000 international-units) of crystalline oestrone at 6 p.m.; 18.9 mg. of crystalline progesterone at 6 p.m.

November 28th, 1935.—18.9 mg. of crystalline progesterone at 9 a.m.; 18.9 mg. of crystalline progesterone at 6 p.m.

November 29th, 1935.—18.9 mg. of crystalline progesterone at 9 a.m.

November 30th, 1935.—No medication.

December 1st, 1935.—No medication.

December 2nd, 1935.—Operation performed at 10 p.m.

A close examination of both ovaries was made during the operation and it was decided by all present that they were of the senile atrophic type without the least evidence of the presence of macroscopic follicles or corpora lutea.

A second case in this series (not reported) received a similar amount of oestrone with three doses of 18.9 mg. of progesterone instead of five doses as in the case here reported. The endometrium was very thick and showed a very pronounced differentiative change. The ovaries in this case contained multiple, apparently active lutein bodies, a circumstance not previously observed by the author. This condition in the ovaries was obviously present before hormone therapy was instituted, and conclusions could not be drawn regarding the effect of the hormones which were administered to this patient.

It is not possible to comment on the individual effect of oestrone and progesterone when the two substances are administered at the same time to one patient. An effort is being made, in our clinic, to observe the effects of the hormones when administered separately to different patients and to continue observations on the effects of smaller doses of progesterone following oestrone therapy.

Comment and Conclusions.

So far as I am aware, no one has previously made an attempt to study the effect of oestrone and progesterone upon the endometrium of the human in the presence of functioning ovaries. The reason is obvious. It is on account of the extreme difficulty experienced in attempting to estimate the effect on the endometrium from the hormones which are secreted by the intact ovaries. Kaufmann[1] has reported results from investigations of this kind in cases of amenorrhoea, and in some castrates. Werner[2] and Collier made the original observations after administration of oestrone (theelin) to women from whom the ovaries had

been removed. These authors administered the hormones over a longer period of time in an attempt to imitate the endometrial development which occurs during a normal menstrual cycle. In our case the hormones were administered over a period of four days and the uterus was removed for study of the endometrium on the third day following the last dose.

In my opinion, the marked increase in the endometrial development in this case was due to the massive doses of oestrone and progesterone. It, therefore, seems reasonable to conclude that large doses of these substances will cause a rapid increase in the rate of the proliferative growth and in the rate of the differentiative changes which occur in the endometrium during the menstrual cycle. This increase in the rate of growth and development appears to be proportional to the concentration of the hormones rather than to the duration of time over which they are administered.

The above conclusions have been supported by results which I have observed in the treatment of amenorrhoea by the administration of the oestrogenic hormones. Uterine bleeding with apparent endometrial degeneration has followed soon after the administration of large doses, while the same effect is frequently not produced by small doses, even when continued over a long period of time. It is my belief that oestrone and progesterone have a very limited value in the treatment of amenorrhoea, because oestrone and progesterone, even in large doses, do not stimulate the ovary, and it is quite possible that these substances inhibit anterior pituitary function in the human being. There is no reason, therefore, why a regular cycle should follow one menstrual period which has been artificially produced by hormone therapy.

The development which was produced in different areas of the endometrium in this case was diverse. Therefore, in the study of hormonal effect on the endometrium, observations made on complete serial sections of the uterus are more accurate than observations made on portions of endometrium which are recovered with a curette.

The author is indebted to Professor G. F. Marrian who prepared the oestrone and progesterone in the pure crystalline form, and to Professor O. Klotz who kindly arranged for the preparation of the sections of the endometrium in his department. It was supported in part by a grant from the Banting Research Foundation.

The oestrone and progesterone were prepared in the Biochemical Laboratories of the University of Toronto. The progesterone was assayed and put into ampoules by the Connaught Laboratories.

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Aetiology of the Toxaemias of Pregnancy.

BY

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IT is extremely interesting to conjecture about the reactions of different women to pregnancy, and also the reactions of the same individual to different pregnancies. The term, a harmonious symbiosis, has been used to describe a normal pregnancy. In the presence of complete harmony, how often one sees a girl, who has never been robust, suddenly develop in physique and fairly to radiate health, such as she has never before known. On the other hand, strong, vigorous, young women, in apparently perfect health, may react so unfavourably that their lives may be lost, or saved only after a desperate illness. Many instances are encountered in which an individual patient reacts very unfavourably to one pregnancy, and in a subsequent pregnancy seems to have a state of complete harmony.

During the last several years, a tendency seems to have developed to leave the aetiology of the toxaemias of pregnancy as a question not capable of any solution. The work of Veit and Schmorl, and the Abderhalden reaction, seemed for a time to be very encouraging. Later research, however, showed that syncytial cells could be demonstrated in the maternal bloodstream in cases which did not show any signs of toxaemia. The uncertainties of the Abderhalden reaction were such that it has been more or less discredited.

Some years ago the suggestion was advanced that lack of consanguinity between mother and child might explain the toxaemias of pregnancy. Some experimental work was done with results which were rather suggestive. Zotterman and Wildner examined a series of 213 cases, and found incompatibility in 26.9 per cent. McQuarrie found 70 per cent incompatible in a series of toxaemic cases, as opposed to 11.4 per cent

incompatible in a controlled group of his normal cases. In a review of McQuarrie's work, C. O. Maland states:

> Although the data submitted in this paper are not sufficient to warrant the drawing of final conclusions, they are very suggestive of the existence of some relationship between the incompatibility of maternal and foetal blood on the one hand and the development of eclampsia or pre-eclamptic toxaemia on the other. Such a theory, however, should be regarded as merely tentative, and cannot be accepted until a satisfactory mechanism has been demonstrated by which the foetal blood can gain access to the maternal circulation. [1]

In 1926 the writer suggested in an article in the *Canadian Medical Journal*, a correlation of Veit's theory, with the later suggestion of a lack of consanguinity.[2]

It is surely a reasonable assumption that if the blood of an individual is incompatible with that of another, that this incompatibility may well be shared by all other body fluids and tissues. Chorionic tissue is foetal in origin. On this basis, syncytial cells in the maternal blood-stream, in a case in which there was consanguinity, would act merely as minute, inert foreign bodies, without producing any trouble. On the other hand, the presence of these cells, in a case in which blood grouping differed, may very well explain the widespread pathology which exists in severe cases of toxaemia. The correlation of these theories explains why there need not be any intermingling of foetal and maternal blood. It also explains eclampsia with hydatidiform mole. Post-partum eclampsia can also be explained on the assumption that a certain amount of chorionic tissue is still retained *in utero*.

An interesting analogy to this theory is the fact that skin from a donor is unsuitable for grafting when blood groupings differ. Another similar analogy was, I believe, suggested by Blair-Bell to explain sterility.[3]

The son of the writer (R. W. Maclellan), who is a medical student at Dalhousie University Medical School, has been interested in the correlation suggestion, and has contributed an extremely interesting suggestion. He suggests that eclampsia should rarely, if ever, occur when the mother is a universal recipient Group 1 (AB), or when the developing foetus is a universal donor, Group 4 (o). The following table should, if this theory is correct, indicate which groupings would develop potential eclamptics:

If blood of mother is	And blood of father is	Then the blood of child will be
1 (AB)	1 (AB)	1 (AB), 2 (A), 3 (B)
	2 (A)	1 (AB), 2 (A), 3 (B)
	3 (B)	1 (AB), 2 (A), 3 (B)
	4 (O)	2 (A), 3 (B)
2 (A)	1 (AB)	*1 (AB)*, 2 (A), *3 (B)*
	2 (A)	2 (A), 4 (O)
	3 (B)	*1 (AB)*, 2 (A), *3 (B)*, 4 (O)
	4 (O)	2 (A), 4 (O)
3 (B)	1 (AB)	*1 (AB)*, *2 (A)*, 3 (B)
	2 (A)	*1 (AB)*, *2 (A)*, 3 (B), 4 (O)
	3 (B)	3 (B), 4 (O)
	4 (O)	3 (B), 4 (O)
4 (O)	1 (AB)	*2 (A)*, *3 (B)*
	2 (A)	*2 (A)*, 4 (O)
	3 (B)	*3 (B)*, 4 (O)
	4 (O)	4 (O)

When the blood grouping of the child is expressed in italics, then the mother will be a potential eclamptic. When the child's group is in roman numerals, the mother will not be a potential eclamptic.

References. The grouping systems of both Moss and Lansteiner have been used. The above table is merely a different arrangement of that found in Todd and Sanford.

I have always tried, clinically, to classify patients in my own mind as potential eclamptics or not, depending on the reaction to pregnancy as evidenced by a feeling of well-being and improved health, on the one hand; or the reverse, with symptoms of lassitude and malaise. According to this theory, the testing of the paternal and maternal bloods should enable us practically to eliminate a very great number of women as not at all likely to have any serious trouble. In the groups in which an unfavourable reaction was probable, extra care and close supervision should go a long way toward preventing the development of severe toxaemia.

A definite determination of the aetiology of the toxaemias of pregnancy, aside from any value from a therapeutic standpoint, would be of the utmost scientific satisfaction and of very considerable biological interest.

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Lithopaedion

BY

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A LITHOPAEDION is a pathological rarity. Kuechenmeister[1] reviewed the literature from 1582 to 1880 and collected 45 authentic cases. More recently Masson and Simon[2] reported nine cases which had occurred at the Mayo Clinic between the years 1903–1926 inclusive. They stated that until the end of 1926 the total number of recorded cases, including the Mayo Clinic series, was 183. Theirs is a most comprehensive contribution to the literature on the subject.

There are several instances of a lithopaedion being retained for a number of years. Mozzetti-Monterumici[3] has published a case of the retention of one within the abdomen for 40 years; Otell[4] had a similar experience; in Voegelin's[5] and Francisco's[6] cases there was retention for 18 and 15 years respectively. Otell's patient died at the age of 75 of an intercurrent disease, and a lithopaedion was a fortuitous discovery at autopsy. The patient was nulliparous, but at 35 had suffered from amenorrhoea for some months.

Both Bland[7] and Watters[8] report cases in which a lithopaedion had been retained 15 and 11 years respectively and in which both patients had had three normal deliveries with the tumour *in situ*. Emmert[9] has had the unique experience of observing the evolution of a lithopaedion. Radiograms were taken at intervals during a period of eight and a half years when the patient was under observation. Operation was refused. At the end of this time the formation of the lithopaedion was complete.

An attempt at classification has been made by Kuechenmeister. He has recognized three types.

1. *Lithokelyphos* (stone-sheath or egg-shell). In this calcification occurs mainly in the membranes. The foetus is uninvolved in the calcifying process.

2. *Lithokelyphopaedion* (stone-sheath child). Both foetus and sac are impregnated with lime salts.

3. *Lithopaedion* (stone child). The foetus is infiltrated with calcium salts, and there is little or no calcification of the membranes. This term strictly should be applied to the cases in which the foetus itself has undergone calcification, having escaped from its membranes into the peritoneal cavity.

Group 3 (the stone-child) is the true lithopaedion, and Group 1 in Kuechenmeister's opinion is the most common.

Recently the writer had an experience of a case which possessed the following features:

On November 27th, 1935, a Chinese patient, aged 34 and married 17 years, came to hospital complaining of dysmenorrhoea and an abdominal swelling. She had had a normal delivery 16 years ago and there was not any history of abortions. Puberty occurred at 17 and amenorrhoea before marriage. Menstruation was of three days' duration, occurring at 25-days' intervals. Ten years ago she had had amenorrhoea for 10 months. During this time there were foetal movements and enlargement of the abdomen. She was convinced that she was pregnant. For three days there were labour pains, and, on consulting a Chinese native doctor, she was told she was in labour and given some opium, which relieved her of her pain without any effect on her abdominal swelling. The latter has slowly decreased in size. She cannot recall having had any bleeding or pain in the early months of her amenorrheoa. Since the false labour 10 years previously she has suffered from menstrual pain and irregularity.

On abdominal examination there was a solid, round, immovable tumour extending up to the umbilicus. *Per vaginam* a hard, irregular mass was felt filling the whole of the pelvis. It was impossible to define the uterus apart.

On November 28th, 1935, laparotomy was performed. A tumour (Fig. 1) was found occupying the pelvic cavity. In parts the omentum and sigmoid colon were adherent to the mass. The uterus was normal in size but raised above the level of the symphysis pubis. The left Fallopian tube was tightly stretched over the tumour and the ovary on that side was not seen. During removal of the mass the left ureter was exposed for some distance. The round ligaments were plicated. Both the right Fallopian tube and ovary were normal in appearance. Convalescence was uninterrupted.

On incising the tumour-capsule one was somewhat surprised to find a calcified female foetus (Fig. 2). The placenta was not to be found, but a portion of the umbilical cord was present. The capsule was intact and not adherent to the foetus, save in the region of the shoulders. The body and limbs were acutely flexed and compressed, and in this way a posture, which occupied as little abdominal space as possible, had been adopted. The measurements of the encapsulated tumour were six inches broad, seven inches obliquely, and four inches high. The unencapsulated foetus measured eight inches from vertex to coccyx. It weighed three and a half pounds. A small incision was made in the gluteal region, and it was obvious that the tissues were infiltrated with lime. A radiogram (Fig. 3) was taken of the foetus unenclosed in its capsule. Several portions of the capsule were examined microscopically. Ovarian tissue was not seen, and the capsule consisted of fibrous tissue with calcified areas.

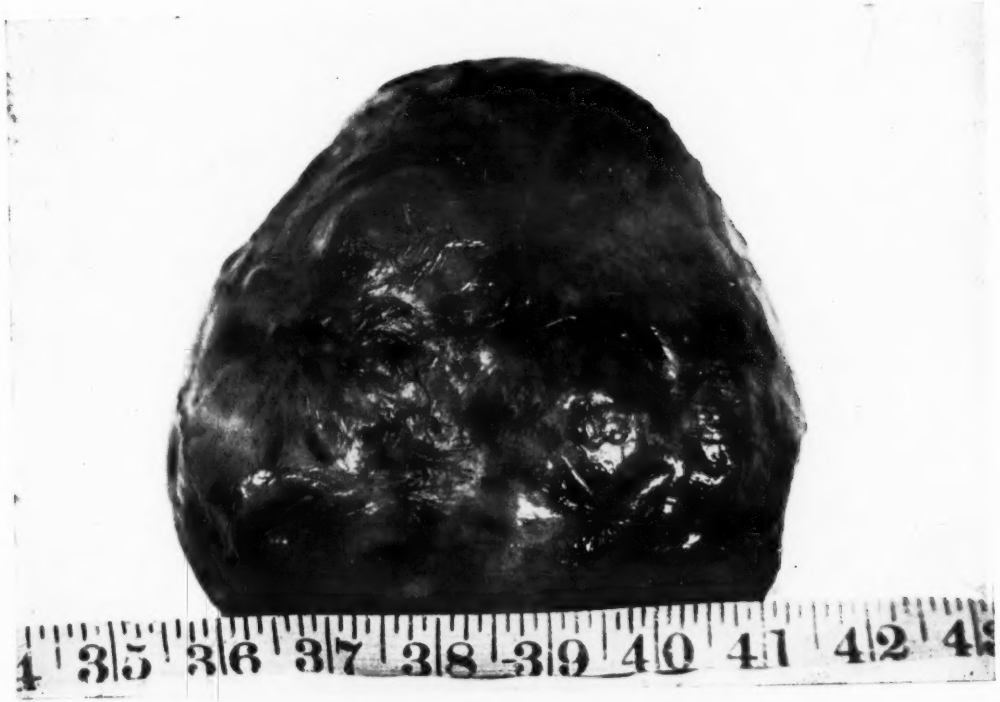

FIG. 1.

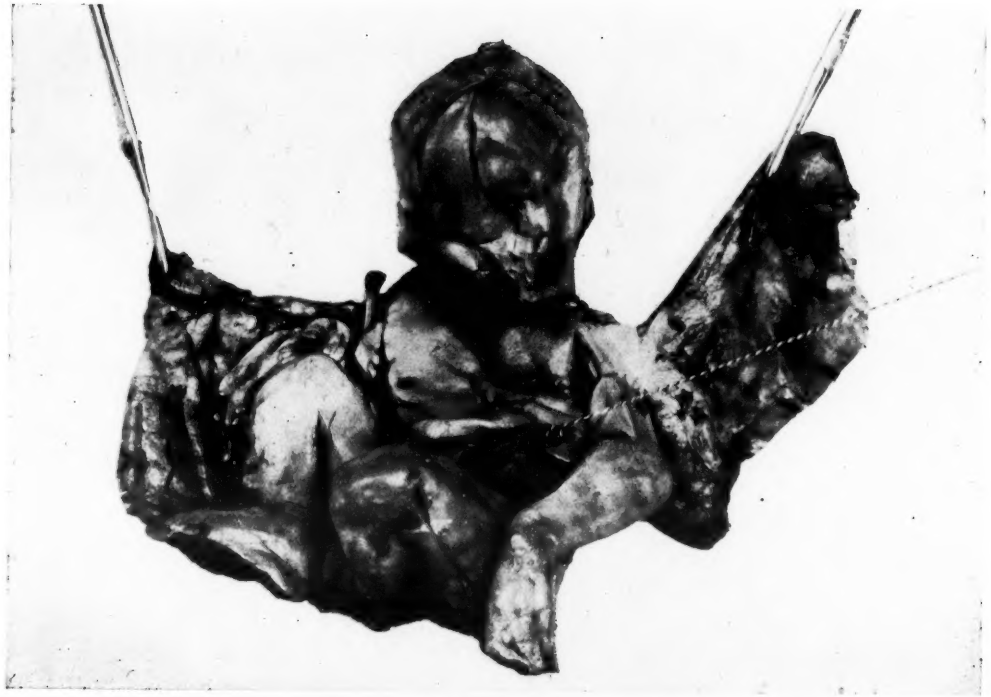

FIG. 2.

FIG. 3.

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Commentary.

A case of lithokelyphopaedion (Kuechenmeister's classification) is reported. This type—the " stone-sheath child "—is the rarest. There was not any history of primary tubal rupture. In most of the recorded cases there is a history of bleeding in the early months of pregnancy.

Menstruation became irregular after false labour. This is a common finding.

The condition is usually diagnosed as a fibroid or an ovarian cyst. In this patient the former diagnosis was made.

The absence of the ovary is unusual. At first, the possibility of an ovarian pregnancy was considered, but as pathological examination of the capsule did not reveal any ovarian tissue this diagnosis was not considered further. The fate of the ovary, in those patients in whom it is absent, is conjectural. In all probability the ovary becomes atrophied by pressure and involved in some absorptive process.

I am indebted to Professor L. J. Davis for the pathological examination and Dr. Farr for the radiogram.

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A Case of Theca-cell Tumour of the Ovary in a Woman aged 92 years

BY

J. H. PATTERSON, M.B., B.Ch., and
W. McK. H. McCULLAGH, F.R.C.S.

THIS case is recorded as an example of a rare ovarian tumour occurring in extreme old age. On going through the literature, it appears to be the oldest recorded case by a wide margin. The case is also of interest as the tumour proved to be of the theca-celled type of the granulosa-cell group of tumours, of which only a few clearly established cases are reported; six were recorded by Loeffler and Priesel[1] in 1932 as *fibroma theca-cellurare xanthomatodes ovarii*. Two cases were reported by Melnick and Kantner[2] in 1934, and they also did not consider them to be a form of granulosa-cell tumour. Plate,[3] Arnold Koener and Mathias[4] have also reported cases. However, one was included by Novak and Brawner[5] in 1934 in their review of 33 cases of granulosa-cell tumour on the grounds of their probable origin from embryonal cell rests in the hilum of the ovary. This is the theory put forward by Robert Meyer[6] in 1915 and now generally accepted as being the best explanation of the widely different histological structures found in different granulosa-cell tumours, and indeed in each individual tumour. Meyer's theory is supported by the work of Fischel[7] and Politzer,[8] who demonstrated that the germinal epithelium and the theca-cell layers both arise from the ovarian mesenchyme, which explains the frequent sarcomatous appearance occurring in many granulosa-cell tumours.

Endeavours to ascribe the origin of granulosa-cell tumours to adult follicular tissue in the ovary have been made by Robinson[9] and Melnick and Kantner, but the frequent occurrence of these tumours in women many years past the menopause, whose ovaries should not contain any granulosal or thecal tissue, does not support their view.

The clinical features of granulosa-cell tumours in old women are well typified in this case, and are all the more remarkable considering the patient's great age. A wide unatrophied vaginal

vault does not appear to have been previously reported in the English and American literature. A history of vaginal bleeding, the large uterus and Fallopian tubes, and the endometrial hyperplasia were marked features of this case, and the light yellow colour and lobulated appearance of the tumour are typical.

Microscopically the sections show very well the oestrogenic hypertrophy of the endometrium with cystic dilatation of the glands, and the structure of the tumour itself is very similar to the illustrations of Melnick's and Kantner's cases, and Novak's and Brawner's case. Decidual changes in the endometrium in cases of the theca-cell type have been reported by Dworsak,[10] Lellbach,[11] and others. The widespread lipoid droplets in all the cells, here and there filling a cell completely, also present a similar picture. A photograph of a section stained for lipoid is not shown, as the droplets are so fine that it would be unconvincing. Luteinization occurs to a varying degree in granulosa-cell tumours. Holmer's[12] case showed very marked luteinization, and the theca-cell tumours all show lipoid droplets. The so-called luteinomata, however, are very difficult to differentiate from hypernephromata and it is possible that some tumours labelled luteinomata, which have been hormonically inactive, have been really hypernephromata.

Although granulosa-cell tumours occur at all ages, it is during old age and before puberty that they are most easily recognized, causing vaginal bleeding, often pseudo-menstrual in type.

In children before the age of puberty the features are most marked, being those of precocious puberty with all the usual manifestations, and also increased skeletal growth. Except for some degree of mammary enlargement, and the persistence of axillary and pubic hair, the signs disappear after removal of the tumour. Eight cases only have been described: E. Novak[13] (three), Bland and Goldstein[14] (one), Meyer[15] (two), Blau[16] (one), and Pahl[17] (one).

In women during active sexual life the clinical features of granulosa-cell tumours are less easily recognized. Excessive irregular uterine bleeding which often follows a period of amenorrhea is frequently the history. The above history and an adnexal swelling led to the diagnosis of ectopic pregnancy being made in a case reported by Schultze.[18]

All the clinical manifestations are due to the production of the hormone oestrin by the tumour. This has been conclusively proved both by observation of results of treatment, and also by investigations carried out by Bland and Goldstein, and Schus-

chania.[19] Meyer reports two cases in post-menopausal women who had galactorrhoea, and in one case in which the endometrium was decidual. Novak and Schultze have each reported cases of patients who had the tumour removed and complained of having to endure menopausal symptoms of the vaso-motor type for the second time.

The malignancy rate in granulosa-cell tumours has been recently reviewed by Novak and Brawner in 1934, and by Murphy[20] in 1935. These recent and careful follow-up schemes show the malignancy rate to be higher than has been previously supposed. Novak's and Brawner's malignancy rate in 33 cases was 28.1 per cent, as opposed to 8 per cent to 10 per cent reported by previous writers.

Case Report.

The patient, aged 92 years, had had seven children, with one living child aged 61 years, admitted in December 1935 for back-ache and vaginal bleeding due to an abdominal tumour the size of a large grape-fruit, which felt like a pedunculated fibroid.

The menopause occurred 36 years ago, at the age of 52. Four years ago slight irregular vaginal losses of blood began, and these latterly became continuous, though worse at intervals. The loss itself in appearance resembled that of a menstrual period. The breasts did not show any signs of activity, though well formed. The patient looked remarkably healthy, physically and mentally, considering her age. The vagina was spacious, the cervix lacerated and unatrophied, the tumour rose to four inches above the umbilicus and was movable; the uterus was large.

Subtotal hysterectomy was performed and both her Fallopian tubes and ovaries were removed. There were not any adhesions except between the tumour, which arose from the right ovary and the uterus.

The patient progressed satisfactorily and was discharged in January, 1936, less than five weeks after admission.

Pathology.

The specimen consists of the uterus, the Fallopian tubes and ovaries. The uterus and Fallopian tubes are enlarged to a size greater than that normal in a parous woman during active sexual life. On section the uterine wall shows hyperplasia and the endometrium is thickened, spongy and raw. The left ovary is replaced by a large tumour measuring six inches by four inches. It is lobulated, well encapsulated and yellowish in colour. On

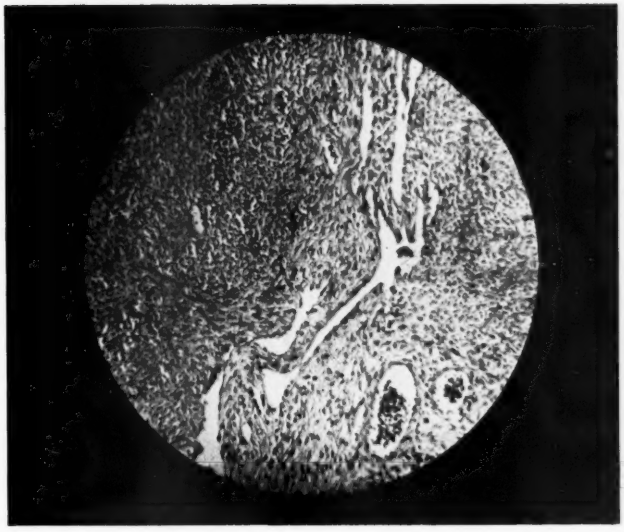

FIG. 2.

Low power. The section is in the region of one of the septa which contains blood-vessels and lymphatics, but the general appearance of the tumour structure and the different types of cells are clearly shown.

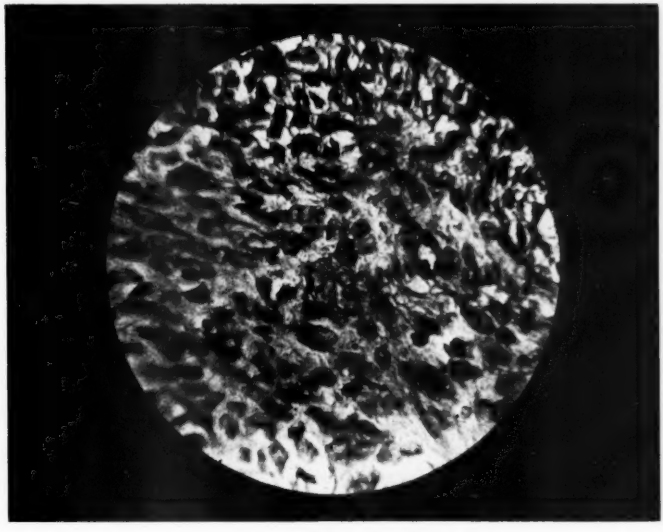

FIG. 3.

High power. The larger epitheloid cells occupy most of the field, but areas of the smaller cells are also shown.

FIG. 4.

The endometrium. The secretory hypertrophy of the endometrium is clearly shown.

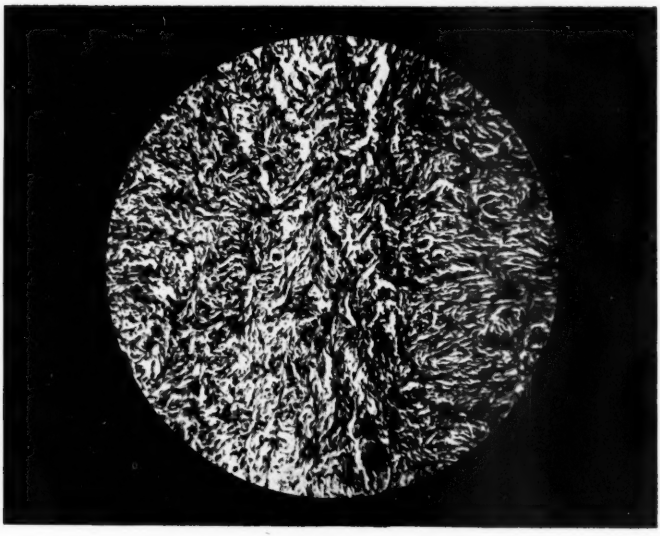

FIG. 5.

The fibroma in the opposite ovary.

the surface of the tumour there are large blood-vessels, and also several thin-walled cysts, half-inch by one inch in diameter, projecting from its surface and containing clear fluid. On section the tumour is of a yellow colour and divided up into lobules by bands of fibrous tissue. The tissue is rather soft and encephaloid in consistence. There are not many cysts in the substance of the tumour.

The right ovary is small and fibrotic and is covered with small clear cysts, about 1 mm. in diameter. From it arises a round smooth hard tumour one inch in diameter which on section is firm and fibrous and does not bear any resemblance to the tumour in the left ovary.

Microscopic Examination.

Low-power. The sections consist entirely of masses of cells, except in places where the fibrous septa seen in the gross section traverse a portion of the section.

The cells are arranged in interweaving bundles with the axes in different directions, the whole appearance resembling that of a very cellular fibroma. Throughout the masses of cells are numerous small blood-vessels and lymph spaces, but there are no cyst formation or Call-Exner bodies.

High-power. The main type of tumour cell is small with a dark staining nucleus. The cells are even in size, and resemble those of the theca-interna layer of the normal follicle. Here and there through the section the cells take on a definitely epithelioid appearance, with more cytoplasm and larger clearer nuclei. Also, in narrow, indefinite and frequently interrupted bands of one or two cells thick, are cells with narrow spindle-shaped dark staining nuclei. These varieties of cells merge into each other without very clear demarcation. Between all the cells there is a fine net-work of collagen connective tissue fibrils. Mitoses cannot be seen, and the nuclei are very uniform in appearance. Other sections from different parts of the tumour show a similar appearance.

Frozen sections stained for fat show all the cells to contain fine droplets of lipoid, and in some places large globules filling the cells are seen.

The Endometrium.

The endometrium shows oestrogenic hypertrophy with cystic dilatation of the glands, and resembles the normal premenstrual endometrium of a young woman, but the hypertrophy is more marked.

The Right Ovary.

The right ovary is fibrotic and the cysts are lined with flattened epithelium. There is some down growth of epithelium from the surface. The tumour is a fibroma which is almost completely hyalinized, the cell nuclei having disappeared in almost the whole width of the tumour.

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Periendothelioma of the Fallopian Tubes*

BY

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MALIGNANT disease of the Fallopian tubes is certainly rare, and I have not encountered a case before. Eden and Lockyer[1] state that 140 primary adeno-carcinomata and 18 cases of chorionic carcinoma have been recorded up to 1928. In 1910 Doran[2] brought his collected cases of "Primary Cancer of the Fallopian Tubes" up to 100, since when about 40 cases have been collected. Doran states that primary sarcoma, primary mixed tumours, and chorion-epithelioma are not included. Burns[3] has reported a case in which thickened and adherent portions of both Fallopian tubes were resected and new ostia established in a woman of 38 years, and these on section proved to be columnar-celled carcinomata of the Fallopian tubes.

Barbour and Watson[4] published "Two Cases of Perithelioma" (1) of the uterus, (2) of the Fallopian tubes. In the latter the left tube and ovary, forming a large adherent mass, were removed, and showed a perivascular arrangement of the endothelial cells.

The specimen under consideration I consider to be one of periendothelioma of the Fallopian tubes. I have not discovered another such case recorded, but I think there cannot be any question about its microscopical characters following in every detail those depicted by Eden and Lockyer[5] as periendothelioma of the ovary.

The specimen shown in Fig. 1 was obtained from Mrs. A. B., a widow, aged 54 years, who had had one child 35 years ago, and in whom the menopause had occurred two years previously.

* A specimen shown at the Manchester meeting of the North of England Obstetrical and Gynaecological Society, January 1936.

She complained of a profuse watery discharge, which was continuous and worse on exertion; there was not any metrostaxis, or pain. The patient was a well nourished woman, and on vaginal examination the uterus was felt anteverted and slightly enlarged with fixed masses on either side of it. Panhysterectomy, involving a difficult dissection, was performed in November 1935, and I learn that the subsequent progress has been satisfactory. The most marked symptom was a profuse vaginal discharge, hydrops tubae profluens, in regard to which Doran[6] states, "In 27 per cent of recorded cases of primary cancer of the Fallopian tubes free watery discharge was a marked symptom." This discharge with fixed masses at either side of the uterus in a woman past the menopause led me to make a diagnosis of disease of the uterine adnexa, probably malignant. This diagnosis proved to be correct. The exact nature of the lesion is, I consider, established from the description of the specimen and its histology, which is as follows:

The specimen consists of the uterus and its appendages removed by pan-hysterectomy, the operation having been performed with some difficulty owing to the presence of firm adhesions of the uterus and its appendages to the rectum and small intestine.

Both Fallopian tubes are seen to be greatly enlarged, and to the touch were solid in consistence.

On bisection the left Fallopian tube is seen to be filled with a whitish growth containing a few scattered areas of haemorrhage. The left ovary has also been bisected and is seen at the edge of the tube. The dimensions of this tube are 8 mm. by 5 mm. by 6 mm. These features are shown in the photograph Fig. 1.

On histological examination the tumour exhibits the usual elements characteristic of these growths. Fig. 2 is a photomicrograph of a section taken from the Fallopian tube at a site marked on Fig. 1. The thin-walled vessels are surrounded by areas of densely staining cells radiating from the vessels. Such appearences are sometimes described as perivascular sarcoma; but from the definite arrangement of the cells radiating from the vessel walls and passing towards the fibrous tissue stroma it seems proper to call this tumour a periendothelioma.

Sections were also cut from the other Fallopian tube and showed the same microscopical features.

A section from the ovary on the left side did not show any evidence of growth; therefore, the specimen is described as one of primary periendothelioma of the Fallopian tubes.

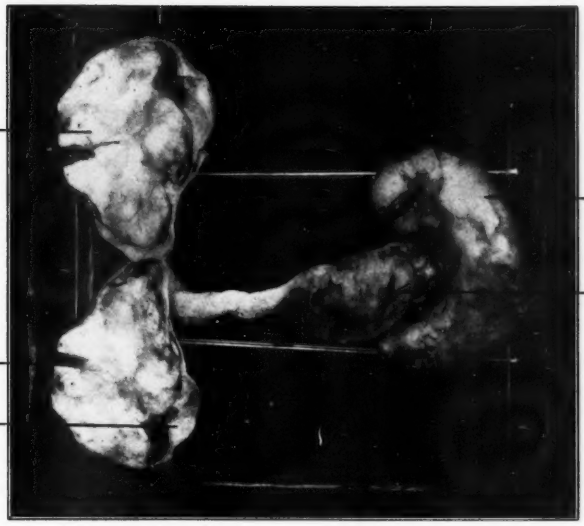

FIG. 1.

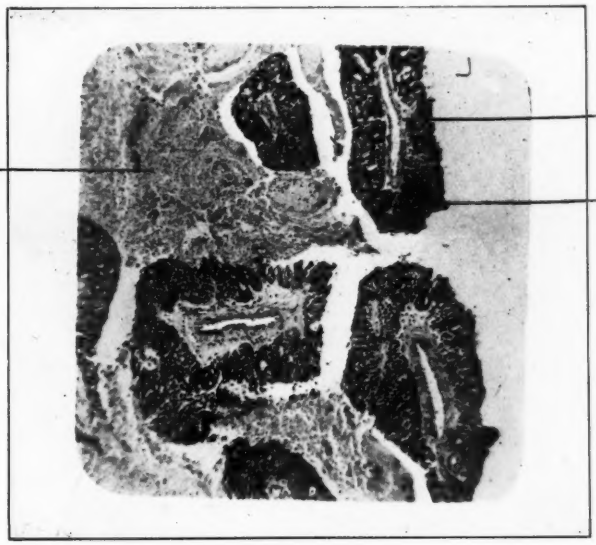

FIG. 2.

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Accessory Lobe of Lung.

BY

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AND

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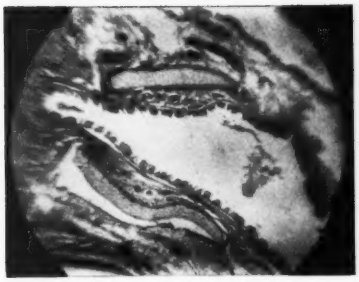
Southern Group Pathologist, Liverpool.

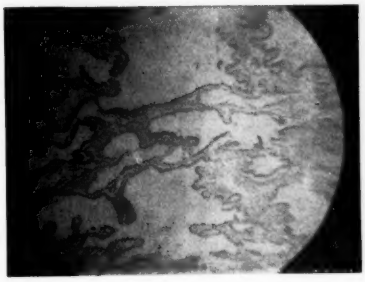
ACCESSORY lobes of the lung are not uncommon. Koontz[1], who collected from the literature all the papers on cysts of the lung and congenital bronchiectases, recorded only 12 cases with accessory lobes. The first was seen by Rektorzik in 1861 in an infant who died of peritonitis on the fourteenth day. In every case the diagnosis of accessory lobe was made after death; in only three cases was the pulmonary tissue cut off by the diaphragm and found in the abdomen, and in one case the lobe was on the right side.

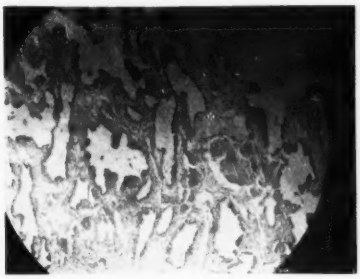
An accessory lobe was found post-mortem in an infant born in the maternity unit of Mill Road Infirmary. At birth the infant appeared normal, but the pulse-rate gradually rose, and cyanosis began to develop on the fourth day. The pulse-rate during the next two days rose to over 150 and became uncountable. The infant became blue, and death occurred on the sixth day. The respirations during the last 24 hours were rapid and shallow.

Post-mortem it was seen that the foetal type of circulation had been re-established, as the ductus arteriosus was patent and the diameter of the vessel was equal to that of the aorta. The foramen ovale was still patent. Judging from the clinical history, the foetal circulation must have terminated in the usual manner and remained normal until the fourth day, when a disturbance of the usual mechanism occurred and the ductus arteriosus enlarged until the bulk of the venous blood was discharged into the aorta. There was a small haemorrhage into the right suprarenal, but not sufficient to cause death. In addition there was a cystic tumour situated between the lower lobe of the left lung and the diaphragm; this tumour was covered by pleura and was pedunculated. The pedicle was attached to the diaphragm and consisted of blood-vessels, nerves

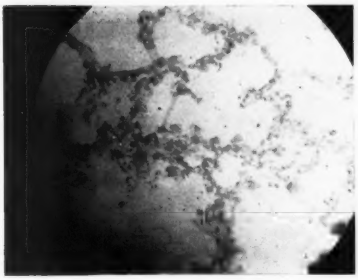


Section of the pedunculated tumour showing a bronchus lined by ciliated columnar epithelium with cartilage plates. (Low power.)





Low-power magnification of cystic lung showing the dilated bronchioli and alveoli. (Alternative prints.)



High-power magnification of the adult type of alveoli.

Photograph from the front showing the cystic tumour cut in half and the peduncle dissected through the diaphragm into the abdomen.

Photograph of viscera showing the cystic tumour of lung with the peduncle and the artery dissected to the coeliac axis. The haemorrhage in the suprarenal and the patent ductus arteriosus can be seen.

Dissection showing the coeliac ganglion giving off two branches and with the artery from the coeliac axis forming the peduncle of the tumour, which is covered by pleura. The patent ductus arteriosus can be seen.

and pleura, but no bronchi were present. The artery was traced through the diaphragm to the aorta at the level of the coeliac ganglion.

Histologically the tumour was composed of recognizable pulmonary tissue. There was a bronchus with cartilage plates, and the bronchioles were prominent because of cystic dilatation. The pulmonary alveolar tissue was relatively small in amount and of adult type. This was rather an anomaly as the tumour was separate from the lung and had not had any communication with the outside air. The change from the foetal type of lung must have been brought about through the excretion of carbon dioxide by the foetal cells lining the alveoli. The presence of the air may account for the cystic dilatation, as there was not much mucus in the bronchus.

Koontz gave a *résumé* of many of the theories which have been advanced in the past to account for the presence of these congenital cysts of lung and congenital bronchiectases. From the nature of this case it was fairly obvious that it was a congenital anomaly, and the pulmonary tissue which was cut off by the pleura during development must have come into contact with the diaphragm, as the blood and nerve supply was drawn from the coeliac axis and ganglion. This was in accordance with Virchow's theory that the ciliated pulmonary cysts are misplaced portions of the respiratory tract. As is so common, there were the other congenital anomalies; the foramen ovale and ductus arteriosus were patent and were responsible for the death of the infant. The presence of the adult type of alveoli might explain the presence of the air which was found in some cysts of the lung by Flemming.[2]

The term "accessory lobe of lung" has been used, but it is not a suitable description, as the lobe is not a functional organ like the accessory spleen or lobe of liver, or the succenturiate placenta. Probably the term "aberrant lobe of pulmonary" more aptly describes the condition.

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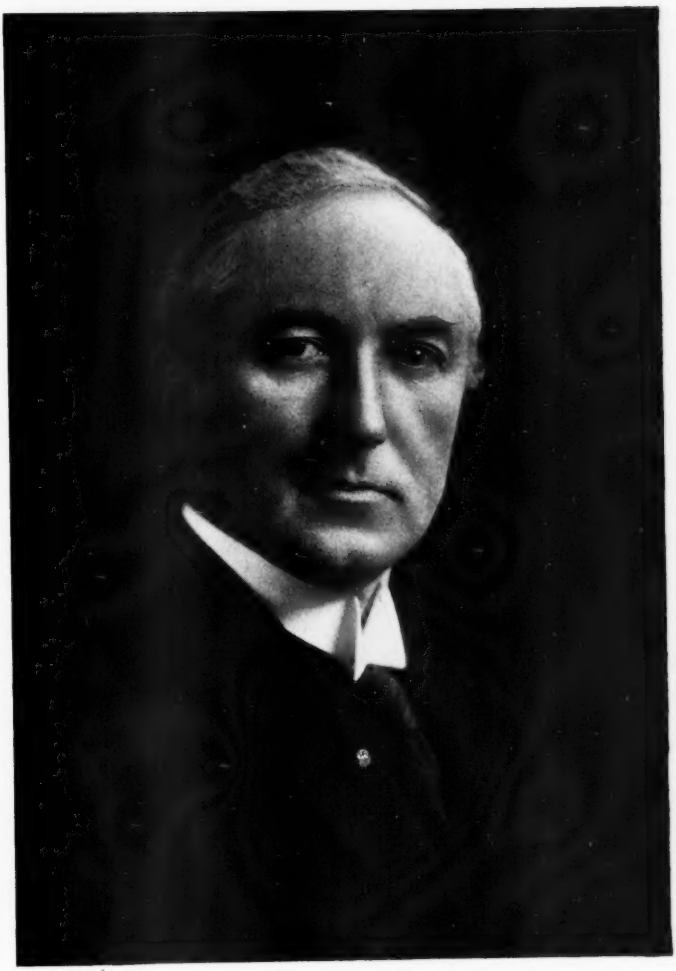
Obituary

JOHN THOMAS HEWETSON

BIRMINGHAM and the midland counties have sustained a grievous loss by the death of John Thomas Hewetson, which occurred at his residence on May 19th. He was a native of Cumberland, and received his early education at Carlisle. He subsequently studied medicine at Edinburgh, Bristol, King's College, and St. Bartholomew's Hospital, graduated with honours at Edinburgh in 1896, and obtained the F.R.C.S. (England) in 1899. In 1901 he took the M.D. of Edinburgh with honours. After a period spent in resident appointments and research work, Hewetson was elected to the Honorary Staff of the General Hospital as Assistant Obstetric Officer under Dr. Thomas Wilson. He held this office for five years, and during this time obtained the Birmingham Ch.M. In 1907 he was appointed on the Honorary Staff of the Maternity Hospital and served there till six months ago. In 1908 he joined the staff of the Women's Hospital and gave up his position at the General Hospital. He was Senior Surgeon to the Women's Hospital at the time of his death, and was one of the original Fellows of the British College of Obstetricians and Gynaecologists.

In Hewetson the medical profession of Birmingham has lost one of its most brilliant members. He was an operator of exceptional skill: calm, decided in action, and possessing unlimited endurance. Few men of his not very robust physique could have achieved the stupendous amount of work that he carried through so easily in his daily routine. A morning spent with him in the theatre revealed his capacity for dealing expeditiously and skilfully with a long programme, at the end of which his usual cheerfulness remained unchanged. There was never a cross or unkind word to any of his team, which made association with him in his work a genuine pleasure. This happy temperament brought him, as might well be expected, a great and devoted following in both private and hospital practice. He had a quite unusual gift of saying the right thing



JOHN THOMAS HEWETSON

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succinctly, and his unerring punctuality in a life of such activity was almost incredible, for he was never late for an appointment.

Hewetson was a true sportsman and a great supporter of cricket and football. He will be deeply mourned by his colleagues, patients and many friends. Our deepest sympathy goes out to his widow and the members of his family.

FREIDA N. LLOYD.

BRITISH COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

THE Quarterly Meeting of the Council was held on Saturday, October 24th, 1936, in the College House, with the President, Sir Ewen Maclean, in the Chair.

Sir Mangaldas Mehta was elected to the Membership of the College.

The following were admitted by the President to the Membership of the College:—

Douglas Allan Abernethy	Oxford
Ida Birchall	Australia
Joseph Rosari Borg	Halifax
William Joseph Clancy	Sheffield
Robert Everett	Blackpool
Francis Harry Hume Finlaison	London
Albert Moor Hartnell	London
Grace Mabel Jones	Cardiff
Henry Andrew Kidd	Halifax
Douglas Marshall Lindsay	London
Muriel Betty McIlrath	Australia
Kenneth Fitzgerald MacKenzie	Hove
David James MacRae	London
George Douglas Matthew	Edinburgh
Robert Baikie Meiklejohn	Canada
John Henry Mulvany	London
Mabel Florence Potter	Bristol
Mortimer Phillip Reddington	London
Ian Munro Robertson	St. Leonards-on-Sea
Marcis Melbourne Rosenfield	Australia
Edynfed ap Iorwerth Rosser	Edgware, Middlesex
Patrick Murries Gordon Russel	London
Ruby Grace Sharp	London
Edward Charles Sugden	London
Arthur MacLennan Sutherland	Glasgow
Raeburn Rodd Talbot	Australia
Joyce Helen Wentworth Wharton ...	Australia
William Wellesley Wilson	Australia

The following were admitted *in absentia* to the Fellowship:—

Rupert Eric Magarey	Australia

and to the Membership:—

Gerald Holmes	Uganda
Phillip Geoffrey Preston	Kenya

HOSPITAL REPORTS.

ROTUNDA HOSPITAL. Medical Report for the year 1934–35, by Andrew H. Davidson, M.D., F.R.C.P.I., F.C.O.G.

THE Report of the Rotunda Hospital is always a very personal document. This year it begins on almost a domestic note. We are told all about the Aga cookers with which the new kitchens are to be equipped, and about the new sluice rooms, bathrooms, and lavatories. The Rotunda is going to be very grand with its one-way traffic arrangements, its brand new mortuary and post-mortem room. "The new out-patient department will be opened in a few weeks' time, and in next year's report I hope to show plans and sketches of its construction." Certainly, now that the building is up there seems no reason why the architects should not go ahead and get the plans drawn!

As in previous years, the Report contains a general review of the work of the past 12 months. In this section the main abnormalities are dealt with in their several groups, and the Master makes detailed reference to individual cases which have been specially instructive. He draws attention particularly to those which have caused him to alter his views on any problem, and he tells us what he proposes to do in the future in the light of his recent experiences. This confession of faith makes interesting reading, but it would be more agreeable if it were framed with a little more regard for grammar and phraseology. Surely it would be a simple matter to improve the following sentences without lengthening them to any extent: "Her first labour was a Caesarean section." "The second case was admitted with a prolapsed cord and neglected shoulder." "There were three bougie and three oil and quinine inductions."

No drastic change has been made in the purely obstetrical methods of treatment, but the Master now prohibits the use of chloroform as an anaesthetic for operative work in the labour room. "There was a chloroform fatality at the beginning of the year in a young healthy patient, and this made such an impression on me that I refused to allow it to be used again as a general anaesthetic. Although this decision is bound to evoke criticism, I feel that it is a wise one." We think so, too, and we believe that the majority of obstetricians will warmly commend it. The only point we would criticize is the decision to use nothing but ether. It is somewhat surprising that gas and oxygen should be excluded, the more so as this anaesthetic is mentioned as being in common use in the gynaecological department.

The staff of the Rotunda took part in the investigation into the suitability of various forms of anaesthesia and analgesia carried out under the auspices of the British College of Obstetricians and Gynaecologists, and their experience of the Minnitt apparatus and of the Christie Brown inhaler coincided with that of other observers. The results of a minor investigation into the use of nembutal and sodium soneryl are also summarized, but in each case the series is too small to give the conclusions any statistical importance.

In discussing the operation of Caesarean section the author explains that

"all cases of disproportion seen in the dispensary are sent into hospital at the thirty-sixth or thirty-seventh week for investigation. Doubtful cases are examined under an anaesthetic and a careful internal Muller Kerr investigation carried out. Premature labour is induced when indicated and also in cases which are border-line at the time of examination. I have no doubt that this is the right policy to pursue, and it is one of the chief reasons for our very low Caesarean section incidence as compared with other clinics." It is obviously the right policy, but we think that the reference to other institutions might well have been omitted. This implication of superiority is evident in several paragraphs, and every now and again the reader is reminded of the gentleman who thanked God that he was not as other men.

Unconsciously, perhaps, the author makes several statements which might be excused in an elementary textbook but which are inadmissible in a report of this kind. For example: "Blood transfusions were given with great benefit to 2 cases of P.P.H. following placenta praevia. This treatment can be a life-saving measure." No doubt, but everyone who is likely to read this Report has been aware of that for a long time. Even more objectionable is the following pseudo-scientific observation: "The additional stirring-up of toxins incidental to labour throws an extra strain on the already damaged organs and is likely to precipitate fits." Does labour stir up toxins? Where does it stir them from? Do we even know with absolute certainty that eclampsia is of toxic origin?

Only one case of uterine rupture was encountered during the year. It is very well described, but in itself it cannot justify the statement that "the conservative method of treatment is often sufficient and usually yields very good results." The author is obviously drawing upon his past experience and upon the recorded observations of other workers. Nevertheless, such a sweeping statement, however true, reads unconvincingly after an account of a single case. In another part of the Report the author tells us that he has "formed the opinion that pubiotomy has a small but extremely useful place in obstetrics." Unfortunately, his results are unlikely to lead others to the same conclusion, for of the six operations performed two were failures. One patient was delivered of a dead foetus, and the other required Caesarean section in the end.

So far the reviewer appears to have done nothing but criticize. It is only fair, therefore, to state clearly that despite the many faults he has found with the Report, it remains a record of great value and of great merit.

The results of the year's work are extremely good, and we must sincerely congratulate the Master and his assistants on the low mortality in both the intern and the extern departments. For the hospital as a whole the death-rate was only 0.29 per cent, and for the indoor cases only 0.43 per cent. The morbidity rate, according to the British Medical Association standard, was 2.9 per cent, an achievement upon which the medical and nursing staffs can justly pride themselves.

LEEDS MATERNITY HOSPITAL. Medical Report for the year 1934, by David W. Currie, M.D., Ch.M., F.R.C.S., M.C.O.G.

THIS Report is noteworthy for the excellence of its summarized case-histories. These short accounts convey very clearly the essential features of the case,

and their value is increased by the comments and opinions which accompany them. They are written lucidly, simply, and gracefully. Ugly expressions and jargon have been avoided, with the result that reports read easily and smoothly despite their brevity.

Many of the cases recorded are of great interest, notably those of peritonitis. These are described along with the fatal cases, and are included in a special review of an epidemic of puerperal sepsis which occurred in the hospital in the course of the year. The source of the infection is discussed fully, and the lessons learned from this unfortunate experience are tabulated.

But, while these features of the Report deserve the highest praise, the utility of the Report as a whole is restricted by the absence of detailed information on the abnormal cases not individually described. It is impossible to include the Leeds results in any statistical analysis, and anyone writing a paper on, say, placenta praevia, cannot augment his control series by including the cases treated in this hospital. This is a pity, as it has been proved that it is not impossible to combine a reasonable amount of letterpress with equally important tables. It is done regularly in the Report of the Rotunda Hospital, and we hope that in the future the Registrar of the Leeds Hospital will adopt this suggestion.

ST. MARY'S HOSPITALS, MANCHESTER. Report of the Maternity Department for the year 1934.

DURING the year under review, 2,438 patients were treated in the wards. Of these cases 1,525 were "booked," 45 were transferred as "emergencies" from the Hospital District, and 868 were "unbooked." The complications encountered were numerous and varied, and the Report is correspondingly full of interest. Considering the difficulties presented, the results were good. In all there were 34 maternal deaths, which represents a gross mortality rate of 1.39 per cent. As always, the rate is definitely higher in the emergency group, the relative figures being 0.52 per cent and 2.53 per cent respectively.

From the first table in the Report it is evident that haemorrhage and shock were at least contributory factors in causing the death of 11 of the fatal cases. Yet from the rest of the tables and from the summarized case-histories we find that blood transfusion was practised on only two occasions. At any rate the procedure is mentioned twice only, although it is possible that this treatment was employed more frequently than the Report would lead us to believe. Surely this must be so, as there were 43 cases of unavoidable haemorrhage, 65 cases of accidental haemorrhage, 14 cases of third-stage haemorrhage, 8 cases of post-partum haemorrhage, 16 cases of ectopic pregnancy, 5 cases of uterine rupture, and 175 cases of abortion, excluding therapeutic and threatened abortion.

There was not any maternal death among the 43 cases of placenta praevia. This is extremely satisfactory. The treatment employed is detailed in tabular form, and embraces all the recognized expedients including Caesarean section, which was performed in 10 of the cases.

Caesarean section was performed on 172 occasions in the course of the year. In the majority of instances the indication was pelvic contraction, but the operation was also chosen in certain cases with a bad obstetric

history, placenta praevia, fibroids, breech presentation, rigid cervix, prolapse of the cord, acute hydramnios, large vesical calculus, toxic albuminuria, and exopthalmic goitre. It is interesting to find that in both booked and emergency cases the morbidity rate was lower after the classical operation than after the lower segment incision.

Labour was induced in 210 patients. Medical induction was selected in 141 cases, and rupture of the membranes only once. The subject of eclampsia is dealt with very fully. The details of treatment are clearly explained, and a splendid table gives the important facts for the entire series of 31 cases. Another interesting table summarizes the clinical features and gives the treatment and results in 24 cases of pregnancy complicated by pelvic tumours.

There is no need to refer to the other matters considered in the Report, as it will be obvious from what has been said that the volume will repay a close study. It is a pity that it has not been found possible to supplement the tables by a brief commentary. This would enhance the value of the Report considerably.

J. Hewitt.

BOOK REVIEWS.

"A Manual of Obstetrical and Gynaecological Pathology." By J. H. TEACHER, M.D. Edited by ALICE J. MARSHALL, M.B. London: Oxford University Press: Humphrey Milford, 1935. Price 45/-, 407 pages.

THE author himself described this book as "In the main an attempt by a general pathologist to record for the consideration and guidance of others the results of 30 years' wrestling with the task of interpreting to the gynaecologist the problems of the endometrium". It is in fact a treatise on the morbid anatomy and histology of the female reproductive organs written by a worker of long experience in that branch of pathology. Unfortunately, Professor Teacher did not live to finish his work. When he died nine chapters had been written, and these have now been arranged and edited by Dr. Alice J. Marshall in collaboration with a number of other writers who have contributed various chapters to complete the work. The chapters written by Professor Teacher comprise about half the book, and deal mainly with the endometrium and its changes during the menstrual cycle and during pregnancy. They unravel that confusion of histological appearances with astonishing clearness and simplicity, and to the histologist who is frequently faced with the task of interpreting curettings this book will be a considerable help. A short chapter on technique is included, in which are described the methods used in the Glasgow Royal Infirmary, with useful information on such points as preparation of curettings for histological examination.

A number of authors have contributed sections. Dr. Alice J. Marshall has added a chapter on the pathology of the Fallopian tube, and Dr. Elinor D. Jackson Rutherfurd two chapters on the ovary. The sections on uterine tumours are very ably dealt with by Professor Matthew Stewart and Professor Gilbert I. Strachan. Dr. Robert Cruickshank supplies a chapter on the bacteriology of the female genital tract including a short description of the Aschheim and Zondek and the Friedmann tests for pregnancy. Professor Hendry has contributed a chapter on ectopic pregnancy, and Professor Fletcher Shaw one on the pathology of the myometrium.

An outstanding feature of this book is the uniform excellence of its illustrations. A large number of microphotographs are included, all of them well chosen and of the highest order. Those illustrating the endometrium are especially good, and even without the text they are valuable and instructive. The need for a book on this subject in the English language has long been recognized, and no one was better qualified to undertake the work of compiling it than Professor Teacher. He was not only an acknowledged authority on gynaecological pathology but he was also a vivid writer on the subject, and his untimely death before the completion of this work has been a serious loss to medicine. A word of acknowledgement, however, is due to those of his colleagues who have so ably helped in completing the book. They have done an excellent work, maintaining a uniform high standard throughout, and have produced a textbook which will take an important place in pathological laboratories.

J.B.D.

"A Manual of Practical Obstetrics." By O'DONEL BROWNE, M.B., B.Ch., F.R.C.P.I., M.C.O.G., Assistant Gynaecologist, Sir Patrick Dun's Hospital, Dublin; Assistant to the Professor of Midwifery, Trinity College, Dublin. Bristol: John Wright and Sons, Ltd. London: Simpkin Marshall Ltd., 1936, pp. 363, 20s.

THIS manual is intended for the student and general practitioner, and is mainly concerned with the practical aspects of midwifery.

The text has been so arranged that the more involved subjects are reached after the essential features of obstetrics have been acquired; this is what one would expect to find in any elementary textbook, and is not an unusual feature as the author claims in his preface.

For the most part the methods of diagnosis and treatment are orthodox, but here and there are statements with which we find it difficult to agree. as, for instance, that vaginal douching is beneficial in primary inertia, that the damaged Fallopian tube should be repaired and conserved in ectopic pregnancy, that all efforts should be made to deliver the hydrocephalic foetus alive, or that a carneous mole never contains any foetal parts.

As was to be expected from a distinguished member of the Dublin school, the unrotated occipito-posterior position is not recognized as a cause of serious dystocia, but the fact remains that in England and on the Continent this abnormality is responsible for a considerable percentage of the difficult cases admitted to hospital. The author is quite right in maintaining that much of the difficulty is due to too early interference, but making every allowance for this, we think that the occipito-posterior is an important cause of dystocia and frequently needs to be corrected before safe delivery can be effected.

Dilatation of the cervix by means of sea-tangle tents is given a prominent place as a means of inducing labour, and the author claims that this method is almost universally employed during the second three months of pregnancy. We find it hard to believe that this is so as we have not seen a tent used for 25 years, and prefer to use a small hydrostatic bag when a slow method of inducing abortion at this period of pregnancy is required.

In a book written for the student and general practitioner more stress might have been laid on the problem of maternal mortality and morbidity and the methods most likely to lead to its solution. For example, something might have been said about meddlesome midwifery and in describing the various obstetric operations some guidance given as to which are within the general practitioner's competence or suitable for carrying out in the patient's own home.

These criticisms in no way detract from the value of the book as a useful guide to the student and practitioner in the difficult and arduous field of practical obstetrics.

Daniel Dougal.

"Postgraduate Surgery." Vol. II. Edited by RODNEY MAINGOT. London: Medical Publications Ltd., 1936. Price £7 10s. per volume,, or £9 9s. set of three volumes.

THIS volume consists of some 1,750 pages, well-printed and on the whole excellently illustrated. As in the previous volume the contributors consist

for the most part of the most experienced of postgraduate teachers, and their writings are well known to the postgraduate student. Wakeley writes with characteristic directness on the head and spinal column, and adds a useful chapter on the salivary glands. Wheeler's contribution on the surgery of the neck will be found to be most helpful.

Love deals with the breast in satisfactory measure, but has not been allowed sufficient space for an authoritative article. There is no estimate of the value of diathermy in mammary surgery, and other points of interest to the practising surgeon have not been touched on.

The surgery of the chest is well presented by Holmes Sellors, and the medical aspect of post-operative chest complications by Sleigh Johnson. The chapter on infection of the hand by Hamilton Bailey is a clear exposition of efficient treatment. In the section on sympathetic surgery, Abel has included so much information that the reader may find it somewhat difficult to separate those procedures which are of recognized practical value from those whose value is less certain. The chapters on the urinary system and on the male and female genital tracts are all satisfactorily complete and essentially practical. The inclusion of chapters on the surgery and the pathology of the suprarenal glands is welcome, and the writings of Broster and Vines will be read with great interest.

The section on infection therapy is a valuable one, but is perhaps somewhat limited in scope, in spite of the introduction of a chapter on the infection treatment of hernia. This last is the only striking departure from orthodox treatment, and its insertion is somewhat surprising. The section on orthopaedic surgery by Buxton is not complete in this volume, but the portion included is to the point and will be one of the most frequently consulted parts of the book. There is perhaps need for amplification or modification of some sections; some of the references, too, do not seem pertinent and others of limited importance, so that adjustment in all these may be advisable in future editions. In the meantime there is no doubt that the Editor has achieved his aim of presenting an excellent account of procedures most suitable for the surgeon of the present day.

W. T. W.

"The Time of Ovulation in Women." By KARL HARTMAN. Baillière, Tindall and Cox. Price 13/6. Published 1936.

THIS monograph of about 200 pages has the first nine chapters devoted to reviewing the present state of our knowledge of the physiology of reproduction among the higher orders of the animal kingdom, in particular among the primates. The last ten chapters are then devoted to a review of the possible methods of ascertaining the time of ovulation among the primates.

The author's association with the *Rhesus* monkey colony of the Carnegie Institute, Baltimore, has given him unique opportunities of studying this problem in this species, and he has certainly been forced to the conclusion that there is a far greater similarity between the physiology of reproduction in these monkeys and that in the human race than was at first apparent. He has established with certainty the existence of definite alternating fertile and sterile periods in the sex cycle of these monkeys, and his impartial

review of our present knowledge of ovulation in the human leads him to the prophecy that more accurate clinical data will reveal similar fertility changes in the human sex cycle. He is rapidly collecting unfertilized and early fertilized ova from the *Rhesus* monkey colony, and has established such a similarity between this material and such similar human material at present available that it will undoubtedly form a far more accurate standard by which to assess the stage of development of early human embryo discovered in the future. He anticipates the discovery in the very near future of the early fertilized human ovum before it has become implanted in the uterine wall.

This book is well worth reading by anyone interested in this problem, if he or she has the time to digest its contents slowly. It is a book that will almost certainly go through further editions, as its subject-matter is of intense interest and many of the experiments quoted have yet to be confirmed by independent workers, and much that is at present theory will soon become established fact.

Alan Brews.

Review of Current Literature.

Director: FREDERICK ROQUES, M.A., M.D., M.Chir. (Cantab), F.R.C.S., M.C.O.G.

THIS Review contains the lists of contents and abstracts of the more important articles from the following journals with which the "Journal of Obstetrics and Gynæcology of the British Empire" exchanges :—

British.—The Lancet; British Medical Journal.

Canadian.—The Canadian Medical Association Journal; Bulletin Médical de Quebec.

Australian.—Medical Journal of Australia; The Australian and New Zealand Journal of Surgery.

Indian.—The Calcutta Medical Journal.

American.—American Journal of Obstetrics and Gynecology; The Journal of the American Medical Association; Surgery, Gynecology and Obstetrics; American Journal of Diseases of Children.

French.—La Gynécologie; Gynécologie et Obstétrique; Bulletin de la Société d'Obstétrique et de Gynécologie de Paris.

Belgian.—Bruxelles Médical.

Italian.—Annali di Obstetrica e Ginecologia; Archivo di Obstetrica e Ginecologia; Revista Italiana di Ginecologia, Bologna.

German.—Archiv für Gynäkologie; Zeitschrift für Geburtshülfe und Gynäkologie; Zentralblatt für Gynäkologie; Monatsschrift für Geburtshülfe und Gynäkologie; Münchener Medizinsche Wochenschrift; Monatsschrift für Krebsbekampfung.

Scandinavian.—Acta Obstetrica Scandinavica.

South American.—Boletin de la Sociedad Obstetricia y Ginecologia de Buenos Ayres.

Japanese.—Japanese Journal of Obstetrics and Gynæcology.

The Review of Current Literature thus keeps the readers of the Journal in touch with current literature throughout the world. At the end of the year an Index of all the subjects contained in the articles of the above journals is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology and Biochemistry.

LIST OF ABSTRACTORS.

London: J. BEATTIE, F.R.C.S.; A. C. BELL, F.R.C.S.; R. K. BOWES, F.R.C.S.; J. LYLE CAMERON, F.R.C.S.; A. H. CHENARD, M.B.; R. L. DODDS, F.R.C.S.; B. GILBERT, Esq., F.R.C.S.; R. C. LIGHTWOOD, M.D.; J. A. MOORE, M.B.; C. D. READ, F.R.C.S. (Edin.); F. ROQUES, F.R.C.S.; R. WINTERTON, F.R.C.S.

Huddersfield: W. E. CROWTHER, M.B.

Leeds: R. H. B. ADAMSON, M.D., AND B. JEAFFRESON, F.R.C.S.

Liverpool: M. DATNOW, M.D.; P. MALPAS, F.R.C.S.; T. N. A. JEFFCOATE, F.R.C.S.

Manchester: R. NEWTON, M.D.

Glasgow: JANE H. FILSHILL; R. SHARMAN, M.D.

The Biochemical Journal.

Vol. xxx, No. 8, 1936.

*The effect of weaning upon the secretion of calcium in the urine of lactating rats. L. I. Pugsley.

THE EFFECT OF WEANING UPON THE SECRETION OF CALCIUM IN THE URINE OF LACTATING RATS.

It was found that when the urine of lactating rats was examined there was an increase in the calcium content. This increase was maintained for four days. A gradual increase in the quantity of calcium in the urine was found from parturition until the tenth day of lactation, after this the calcium excretion was diminished. Removal of the mammary tissue from rats lactating for 10 days did not result in an increase in the excretion of calcium. It is concluded that the increase observed upon weaning lactating rats is due to the resorption of milk from the involuting mammary gland.

J. A. Moore.

The Clinical Journal.

Vol. lxv, No. 7.

*Vaginal discharges. A. Gough.

*Unusual accidents in association with placenta praevia. C. M. Marshall.

Vol. lxv, No. 8.

Haemorrhage in early pregnancy. A. M. Claye.

VAGINAL DISCHARGES.

The diagnosis and treatment of the common non-haemorrhagic vaginal discharges is discussed. Examination of the discharge should include an estimation of the degree of acidity, examination of a Gram-stained film, and a culture. A drop of fresh discharge in saline should be examined for trichomonas vaginalis.

PLACENTA PRAEVIA.

The clinical reports of two cases of placenta praevia are described. Spontaneous rupture of the uterus occurred in one case; this was recognized only after the insertion of the hand prior to manual removal of the placenta. In the second case a stomach tube used for the induction of labour was passed through the uterus into the bladder. It is supposed that the stomach tube came in contact with the adherent edge of a lowly implanted placenta and was turned forward through the thinned-out lower uterine segment into the bladder.

J. A. Moore.

The Journal of Physiology.

Vol. lxxxvii, No. 3.

*The effect of vitamin E on the thyroid gland of the rat. E. Singer.

Inhibition of water diuresis by extract of the posterior lobe of the pituitary and its relation to the water load of the body. M. Pickford.

THE EFFECT OF VITAMIN E ON THE THYROID GLAND.

Hypoplastic changes were found on histological examination of the thyroid glands of rats which were deprived of vitamin E. Anterior lobe pituitary extract caused a slight decrease in the colloid content of these glands. The administration of iodine had no effect upon the histological appearances of the gland in the vitamin-deprived rats. Pregnancy produced no significant changes in the microscopic appearances of the thyroids in either normal or in vitamin-deficient rats. Females which recovered fertility after a prolonged period of deficiency and sterility exhibited thyroids histologically similar to the normal hypoplastic gland.

J. A. Moore.

The Canadian Medical Association Journal.

Vol. xxxv, No. 1, July 1936.

*The association of pregnancy, hypochromic anaemia and achlorhydria. J. R. Goodall and R. Gottlieb.

*Presacral sympathectomy as a treatment for obstinate dysmenorrhoea. Nathan Shaul.

*A case of recto-vaginal fistula and stricture of the rectum due to lymphogranuloma inguinale. H. W. Johnston.

ASSOCIATION OF PREGNANCY, HYPOCHROMIC ANAEMIA AND ACHLORHYDRIA.

The association of these three conditions is of very common occurrence and their interdependence is indisputable, but the underlying initial cause is entirely obscure, as is, also, the aetiological association of pregnancy.

In nulliparous women hypochromic anaemia is rarely encountered, and it is, therefore, to be presumed that pregnancy is a definite cause, and as pregnancy is associated with great endocrine disturbance these changes are possibly the cause of the condition of the blood.

The disease is confined almost exclusively to women of middle age. It is characterized by pallor, weakness, atrophy of the tongue, brittle finger nails, achlorhydria and a blood-picture depicting a low haemoglobin content, without a corresponding decrease in the number of red blood-cells. It is insidious in onset which may vary from two to 20 years, with an average of eight years.

A study was made of 200 consecutive non-selected cases of pregnancy in all of which a haemoglobin estimation and cytological blood examination were made. In 115 of these cases analysis of the gastric contents was undertaken during starvation and again one hour after the ingestion of toast and tea.

The findings were considered (1) from the duration of the pregnancy and (2) from the number of previous pregnancies. The haemoglobin content varied from 80 per cent (11.20 g.) in the first, to 75 per cent (10.50 g.) in the second, and to 65 per cent (9.10 g.) in the third, trimester. The reduction of red blood-cells was moderate and not so marked as the reduction in haemoglobin. The average red blood-cell count varied from 4,300,000 in the first, to 4,100,000 in the second, and to 3,700,000 in the third, trimester.

The colour index became relatively lower with increasing anaemia. Analyses were made of the gastric contents of 115 patients, 60 being antepartum and 55 post-partum. During the first trimester normal gastric acidity was found in 50 per cent of the cases; hypochlorhydria in 40 per cent, and achlorhydria in 90 per cent of the cases. During the second trimester hypochlorhydria occurred in 13 per cent and achlorhydria in 87 per cent of cases. During the third trimester normal acidity occurred in 0.5 per cent, hypochlorhydria in 3.5 per cent, and achlorhydria in 96 per cent of cases.

Of the foregoing cases 85 per cent had estimates made of the gastric acidity which tended to return to normal within a week following delivery and large quantities of acid were present. In 12 per cent of the cases only a slight return was noted, and in three per cent achlorhydria persisted.

All of the patients with diminished hydrochloric acid were women who had had rapidly recurring pregnancies. A small number of cases was examined one month after delivery and two per cent of these showed persistent achlorhydria.

Although the number of cases under observation is not large, treatment with ferrous carbonate in large doses has been markedly successful in improving the condition of the blood and relieving many of the distressing secondary symptoms of pregnancy.

A considerable bibliography is appended.

PRESACRAL SYMPATHECTOMY AS A TREATMENT FOR OBSTINATE DYSMENORRHOEA.

Jaboulay, in 1898, attempted to relieve pelvic neuralgia by severance of the pelvic sympathetic nerve chains. His results were not outstanding and these therapeutic measures lay in abeyance for many years.

Leriche, in 1925, after an anatomical study of the pelvic nerves, divided the sympathetic meshes around the internal iliac arteries to relieve dysmenorrhoea. This procedure met with wide acceptance.

Cotte, also, in 1925, practised a simpler operation such as removal of the superior hypogastric plexus, or presacral nerve of Latarjet, for the relief of functional dysmenorrhoea and pain associated with inoperable carcinoma of the uterus. His results were said to be outstanding. In 1931 Cotte reported upon the remote results of the operation in 36 cases; 22 of these suffered from functional dysmenorrhoea, while in 14 there were, in addition, definite pathological processes. Relief was obtained with one exception only. Three subsequently became pregnant and were delivered without mishap.

The operation has been widely practised in the United States of America for the relief of pain associated with inoperable cancer and for obstinate dysmenorrhoea.

A full description of the anatomy and technical details of the operation and a report on three cases is given. An extensive bibliography is appended.

A CASE OF RECTO-VAGINAL FISTULA AND STRICTURE OF THE RECTUM DUE TO LYMPHOGRANULOMA INGUINALE.

Lymphogranuloma inguinale, called by Stannus "the sixth venereal disease", is probably identical with "esthioméne" of the old textbooks.

The disease was discovered by Durand, discussed by Nicolas and Favre, and its diagnosis rendered accurate by the intradermal test of Frei (1925).

The author is of the opinion that there is widespread involvement of the anal, pelvic and rectal glands as well as those of the inguinal region together with extensive stricture of the rectum.

The case reported is that of a woman of 25 years of age, with one child; the menstrual history was normal. The first symptoms were lower abdominal pain and rectal distress. The inguinal glands on both sides were swollen, and after about four weeks from the time of onset two of the glands broke down and discharged yellow pus. Two weeks later, during which time the rectal discomfort increased, there was sanguineous discharge from the rectum. Examination revealed many discharging sinuses in the inguinal and saphenous regions. There was marked tenderness over the lower abdomen, and large pelvic masses in the region of the greater vessels were discovered on vaginal examination. The uterus was not in any way fixed. About three inches above the anus there was a recto-vaginal fistula and about half-an-inch below this level there was a well-marked stricture of the rectum. The rectal wall was much thickened, tender to pressure, and there were three or four nodules in the recto-vaginal septum.

Extensive enquiry revealed that the husband also suffered from inguinal abscesses and sinuses. Frei's test on both husband and wife was positive. Wasserman's test was negative, and bacteriological examination of urethral, vaginal, cervical and rectal smears was negative for gonococci. Investigation with a barium enema confirmed the presence of a rectal stricture, the descending colon, however, was free.

The patients were treated by the intravenous injection of tartar emetic in the strength of one per cent in saline solution. The initial dose was two cubic centimetres, increasing to seven cubic centimetres twice weekly. Little reaction followed the injections, and at the end of six weeks, having received 75 cubic centimetres of solution, the rectal discharge had ceased, and the pelvic pain had subsided.

Fourteen months after the time when first seen, examination revealed a stricture of the rectum which was very tender, the nodular mass in the rectal wall and the pelvic masses had disappeared and the sinuses had healed. A tortuous recto-vaginal fistula remained. The Frei test was still positive and will probably remain so permanently.

J. Lyle Cameron.

The Calcutta Medical Journal.

Vol. xxx, No. 5, November 1935.

Observations on the treatment of the toxaemias of pregnancy. Nemai Krishna Banerjee.

Vol. xxx, No. 9, March 1936.

*Malaria as a complication in pregnancy. A case report. Sudlangsu Kumar Ghose.

Vol. xxx, No. 10, April 1936.

Some atypical cases of eclampsia. Nemai Krishna Banerjee.

MALARIA AS A COMPLICATION IN PREGNANCY. A CASE REPORT.

The patient was admitted with a diagnosis of acute yellow atrophy of the liver. The patient, being in labour, was treated by intravenous injections of glucose, but died shortly after delivery.

The diagnosis of malaria was first made shortly after death by a blood-smear. Post-mortem examination showed the maternal liver and spleen to be grossly infected with malarial parasites. The transmission of the parasites to the foetus through the placenta could not be studied adequately, as although blood-smears from the cord and heart of the dead child showed no parasites, the sections of the placenta, the foeal liver and the foetal spleen could not be studied owing to their being spoilt by an accident in the laboratory.

A. C. Bell.

The American Journal of Obstetrics and Gynecology.

Vol. xxx, No. 2.

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*Cancer of cervix and vagina in a case of complete procidentia. Leo. Brady.

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*Tuberculous endometritis. M. W. Diethelm and T. L. Ramsey.
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The contributions of Great Britain to gynaecology and obstetrics. B. M. Auspach.

A study of a new and potent ergot derivative, ergotocin. F. L. Adair, M. E. Davis, M. S. Kharasch, and R. R. Legault.

*Theca cell tumours. S. H. Geist.

Some newer aspects of reproductive physiology. Emil Novak.

Experiences with amniotin in the treatment of gonococcal vaginitis in children. R. W. TeLinde and J. N. Brawner.

Protein stabilization in pre-eclampsia and eclampsia. Boyd Harden, W. S. McEllroy, and R. R. Huggins.

The treatment of dysmenorrhoea by presacral sympathectomy. F. E. Keene.

The place of colpectomy in the treatment of uterine and vaginal prolapse. L. E. Phaneuf.

Analysis of end-results of labour in primiparae after spontaneous *versus* prophylactic methods of delivery. A. H. Aldridge and Paul Watson.

*Clinical and bacteriologic observations in trichomonas vaginitis. E. Allen, Ll. B. Jensen, and I. H. Wood.

Hypothyroidism as a problem in women. C. H. Davis.

Toxaemia of pregnancy. J. R. Goodall.

Ovary-stimulating factors and antihormones. C. F. Fluhmann.

Recent advances in hysterography. T O. Menees and J. D. Miller.

*When is surgery indicated in retrodisplacement of the uterus? G. H. Gardner.

Selected abstracts: Radiography and radiotherapy.

A Parallel Study of Labour in Young and Old Primiparae.

Because of the general opinion among the lay public and medical practitioners that delivery in an elderly primigravida is more hazardous, Nathanson analysed, on a comparative basis, the first labour in the young and old. In order to get a good comparison he chose 17 to 20 as the age-limit of a young primigravida and 35 to 46 as that of the elderly, taking 186 consecutive cases for each group. In the young group the largest number of cases, 72, occurred at 20 years, while in the elderly group the largest number, 56, occurred at 37 years; 27 cases were in patients over 40 years old.

He found that a high percentage of normal pelves occurred in the old primigravidae, but where an abnormal one was found it tended to be of the funnel type in the elderly group and of the generally contracted (*justo-minor*) type in the younger group.

Occipito-anterior position occurred in 85.71 per cent of the young primigravidae, while in the older cases it was 71.33 per cent. However, occipito-posterior position of the persistent type was twice as frequent in the old primigravidae as in the young ones, 21.94 per cent and 10.28 per cent, respectively. The figures for breech presentation were 6.09 per cent in the old patients and 3.42 per cent in the young, again nearly twice as frequent. Only a very low incidence of the less frequent malpresentations was fouhd. Practically no difference was found in the average duration of pregnancy in the two groups, although it has been asserted that it tends

to be longer in the old primigravida. The author found the statement that the duration of labour among old primigravidae is usually longer to be definitely substantiated in his series, as his figures were 17 hours 12 minutes and 12 hours 48 minutes respectively.

Labour terminated spontaneously in 11.83 per cent of the old patients and 31.21 per cent in the young ones, while prophylactic low forceps was employed in 46.77 per cent of the older patients and 53.76 per cent of the young. Mid-forceps operations were used in 20.46 per cent of cases of the elderly and 10.21 per cent in the young. Breech extraction was also twice as frequent in the elderly, 5.93 per cent, as compared to 2.68 per cent.

Caesarean section was performed in 20 cases, i.e. 10.75 per cent, of the old group, while no patient in the young group had to be delivered in this manner. The author points out that in practically every case Caesarean section was indicated for more than one reason, the most important of which was *not* the advanced age of the patient; such factors as varying degrees of pelvic deformity, non-yielding cervix, pelvic neoplasms, progressive toxaemia, etc., are noted in practically every case. The incidence of Caesarean section of other writers as reported by the author varied from 7.76 per cent to 23 per cent.

Primary uterine inertia occurred in six cases of the old group, and was entirely absent in the young patients; secondary inertia occurred in three elderly patients and in only one of the young group. Thus inertia occurred in 4.83 per cent of elderly primigravidae and in 0.53 per cent of the younger ones.

There were no maternal deaths in the young group, but three elderly patients died—two of haemorrhage and one of failing renal function.

Toxaemias of pregnancy were found to be rather more common in the elderly group, and antepartum haemorrhage did not occur at all in either group in this series.

From this study the author is of the opinion that every case of elderly primigravida should be treated on its merits, but that if a complication develops which might increase the risk of obtaining a dead child Caesarean section should be performed.

HORMONIC INDUCTION OF MENSTRUATION IN AMENORRHOEA OF THREE MONTHS' TO NINE YEARS' DURATION.

Dunn describes five cases of secondary amenorrhoea treated with progynon B (benzonated). He used large doses in order to relieve associated symptoms, such as obesity, menopausal symptoms, melancholia, and migraine, and found that in each case the therapy resulted in the recommencement of the menstrual loss as well as an improvement in the associated symptoms. Ten thousand rat-units weekly were sufficient to bring about a flow within one to three months in two cases; in one case he administered 2,000 rat-units every three days for one month; in one case he gave 10,000 rat-units twice a week for four weeks and then 80,000 rat-units spread over 16 days; and in a case of amenorrhoea of nine years' duration the author obtained three consecutive periods after the administration of 1,126,000 rat-units in a period of 128 days.

He found that the influence of this hormone resulted in inducing hypertrophic changes in hypoplastic uteri and breasts, that it improved the

associated melancholia and migraine, and was non-toxic in extremely high single and accumulative dosage.

A Series of 627 Vaginal Hysterectomies Performed for Benign Disease with Three Deaths.

The superiority of vaginal hysterectomy over abdominal hysterectomy in certain cases is gradually being recognized, and this report of 627 cases with a mortality of 0.47 per cent will add still further to its claim. Heaney reports the indications as being: fibromyoma in 338 cases, uncontrolled menorrhagia 119 cases, prolapse of the uterus 76 cases, adenomyoma of the uterus 60 cases, and the remaining 34 cases for odd conditions. He has never had to abandon the vaginal route and complete the operation abdominally. Of the three fatal cases, one died of peritonitis, another of intestinal obstruction, and the other of pulmonary embolus. There were five cases of post-operative haemorrhage, one of which needed laparotomy for the ligature of a tiny vessel. In seven cases the operation was performed for an adenomyoma involving the recto-vaginal septum, but in only one of these was a hole made in the rectum; this was sutured and convalescence was uneventful. In three cases the vaginal vault opened and a Fallopian tube prolapsed during the convalescence. It was treated by traction on the tube in order to deliver it completely into the vagina; a ligature was then tied round the mesentery and the tube was removed by being burned off with a light nasal cautery. No case suffered from shock or acute dilatation of the stomach, and except for the three fatal cases, no case occasioned the slightest amount of anxiety.

Cancer of Cervix and Vagina in a Case of Complete Procidentia.

Most gynaecologists believe that malignancy rarely develops in the prolapsed uterus, but Brady quotes Emmert and Taussig, who found four cases of malignancy in 10 cases of complete prolapse, and describes a case of his own. The whole of the vagina was lying outside the vulval orifice and the uterus was lying in the vaginal sac—a case of true procidentia. The cervix was replaced by a hard indurated ulcer, and on the left lateral wall there was a second slightly larger ulcer. Both ulcers showed definite squamous-cell carcinoma on microscopic section. Vaginal hysterectomy with extensive removal of the vaginal walls was performed. Because the author had never seen a similar case before, he followed up the after-histories of 56 cases of prolapse in which the interposition operation had been performed at the Johns Hopkins Hospital. In some of these cases a portion of the elongated cervix had been removed—an inadequate operation if cancer was present, as he points out—but not in any case had the patient developed a carcinoma. The author is of the opinion that cancer rarely develops in the prolapsed cervix but that the possibility must never be forgotten.

Cancer of the Female Urethra.

As only 167 cases of primary carcinoma of the urethra have been reported, Auer maintains that such a lesion must be rare. However, he is convinced that there are many cases not reported and that this figure is not a true one. He describes 22 cases with an average age of 54 years. No special predisposing factor was found, although a urethral caruncle preceded

the cancer in several of these cases. The point of origin appeared to be situated on the posterior wall near the orifice, as in practically every case, whether early or advanced, this part of the canal was diseased. Pain on micturition and burning on micturition were the chief complaints followed by frequency and finally pain and bleeding. In this series there was one primary melanoma and two adenocarcinomata, the remaining cases were squamous-cell carcinomata.

The author now believes that the Basset operation, local removal or radiation and removal of lymphatic glands from both groins, is the treatment of choice. He found that the size of the local lesion gave no clue as to the involvement of the glands.

Of this series of 22 cases, nine were classified as early. Two patients refused treatment, six had only local treatment, and one had local treatment with Basset's operation. Of these, two lived more than five years, and one with only local treatment died of glandular metastases after four years. Four cases have been treated less than five years and all are well and apparently free of growth.

Five advanced cases were treated, one had radium locally and is alive after two years; the other four had local treatment and Basset's operation, three are alive after two, five and 12 years respectively, and the other died after 10 years of cancer of the breast.

The remaining eight cases were considered hopeless when seen, all were given palliative radiation and all died within six to 12 months.

THE TREATMENT OF THE PERSISTENT OCCIPITO-POSTERIOR POSITION BY 180 DEGREES MANUAL ROTATION OF THE OCCIPUT.

Rosenfeld describes the Pomeroy technique for manual rotation of the head in cases of persistent occipito-posterior position. The main idea of the manoeuvre is to rotate the head through 180 degrees. This causes the shoulders to change from one oblique diameter to the other without any actual manipulation of the shoulders, and thus prevents a recurrence of the malposition. The details given by him correspond exactly to those taught in some of the larger English schools, and the Abstractor is in agreement that if this technique was more universally used there would be fewer cases of failure of manual rotation.

COMPLICATIONS FOLLOWING CAUTERIZATION OF THE CERVIX UTERI.

The authors describe three cases of widespread pelvic infection following cauterization. In two cases there is a note that curettage was performed as well, and probably the same procedure was done in the third case. It is probable that the spread of the infection followed the curettage rather than the cauterization of the cervix. It is a well-known fact that intra-uterine manipulations, when active infection is present, often leads to generalized pelvic spread, whereas it is difficult to see why the opening and drainage of infected cervical glands with the cautery could lead to such a catastrophe.

TUBERCULOUS ENDOMETRITIS.

There is a wide divergence of opinion at present as to the rarity of tuberculous endometritis apart from that accompanying widespread disease

of the Fallopian tubes, so the report of this case and the opinion of the authors are of great interest. They describe the case of a patient, aged 20 years, who complained of menorrhagia and dysmenorrhoea six months after an incomplete abortion. Nothing abnormal was felt on pelvic examination under general anaesthesia and diagnostic curettage was performed; numerous typical tubercles and tubercle bacilli were found. She refused hysterectomy, but six weeks later was readmitted with bilateral tubal swellings, and when hysterectomy was performed the peritoneum was studded with tubercles. This case teaches us that all curettings for menorrhagia should be examined microscopically. Tuberculosis of the endometrium might then be found to be a less rare disease than is commonly supposed. When tubercles are found hysterectomy should be performed with the least possible delay.

THECA-CELL TUMOURS.

Geist reports in detail five cases of theca-celled tumour of the ovary. Four of the five cases occurred after the menopause and one at the age of 21 years. In one of the two more recent cases hormonal investigation was carried out. The tumour was unilateral and gave rise to typical bleeding—post-menopausal in all cases except of the young married girl in whom there was a history of bleeding for one year followed by a period of amenorrhoea. In all cases the uterus was enlarged and the endometrium thick and active. The tumour was usually hard, and at first sight looked like a fibroma but without its characteristic ascites. There was a tendency to cystic degeneration, and in one case the tumour was described as a thick-walled cyst. The colour was usually yellowish-white, which was due to the presence of varying-sized yellow cellular islands separated by finer or coarser tissue bundles. In some cases the yellow areas were so small that they only showed as pin-point areas in a mass of thick white hyaline tissue. Histologically the yellow areas were composed of plump spindle or polygonal cells with a central or sometimes eccentric nucleus which stained darkly and was rich in chromatin. The cell protoplasm was vacuolated and contained fat. This fat was proved by microscopical and polariscopic investigation to be cholesterol and cholesterol ester and not degenerative in origin. It was limited almost entirely to the cellular elements of the tumour. The tumour, investigated for oestrogenic hormone, was found to contain one mouse-unit per 0.75 grm. of tissue extracted; other types of ovarian tumours which were investigated did not demonstrate any hormone. The author is of the opinion that this oestrogenic content accounted for the active endometrium and the symptom of post-menopausal bleeding in the elderly patients and the amenorrhoea in the young girl. In no case of this series was there any suggestion of malignancy but Löffler and Priesel reported one of their cases as being definitely malignant.

CLINICAL AND BACTERIOLOGICAL OBSERVATIONS IN TRICHOMONAS VAGINITIS.

The authors discuss the problems of trichomonas vaginitis, especially with regard to the bacteriology of the discharge, the mode of primary infection and the possible complications of the disease In one case in which trichomonas were observed in the discharge the patient also com-

plained of a monarticular rheumatism. A streptococcus was isolated from the vagina and was found to be of the arthrotropic variety. Eighty per cent of their cases were cured with various therapeutic measures. On investigating the other 20 per cent the authors found that the infection was temporarily cured but recurred. Most of the patients were married women, and on investigation of the husband the prostatic secretion contained either the trichomona or a streptococcus identical with that found in the vagina of the wife. They are of the opinion that the associated streptococcus is of as much, or even greater, importance in these resistant cases, and suggest that everything must be done to increase the local and general resistance of the individuals concerned.

WHEN IS SURGERY INDICATED IN RETRODISPLACEMENT OF THE UTERUS?

This vexed question is tackled by Gardner, but not answered very conclusively. He divides his cases into two main groups, (*a*) 83 cases, 57 per cent, in which the retrodisplacement is obviously responsible for symptoms and is termed "essential displacement," and (*b*) 62 cases, 43 per cent, in which it was apparently only an incidental feature of more important associated pelvic disease and consequently termed "incidental displacement". This classification appears rather unconvincing, as in both groups such important complications as endometriosis and adhesions are given as associated lesions; certainly, he includes in the second group retroversion incidental to vaginal and uterine prolapse and such conditions as appendicitis and large ovarian cysts. He concludes that retroversion alone may be responsible for lower abdominal pain and pelvic discomfort, uterine bleeding and dysmenorrhoea. Also that the displacement is a menace to the health of the ovaries, which tend to become large, oedematous and cystic, probably the result of altered blood-supply. The author's main method of treatment was a Baldy-Webster operation on the round ligaments and suturing together the relaxed utero-sacral ligaments. In 85 per cent of cases he obtained complete symptomatic relief and an excellent clinical result, four failed to report for examination, and two died from pulmonary embolism. Not in any single case had the uterus returned to a retroplaced position, but seven patients had a slight sagging of the uterus. In 15 cases defundation of the uterus was performed when further pregnancies were impossible or inadvisable. The author came to the conclusion that this operation was followed by post-operative complications more frequently than any other.

B. Jeaffreson.

Journal of the American Medical Association.

Vol. cvii, No. 3, July 18th, 1936.

Trends in American obstetrics during the first third of this century. (Chairman's address). Lyle G. McNeile.

Vol. cvii, No. 4, July 25th, 1936.

The present status of oxytocics in obstetrics. M. Edward Davis, Fred L. Adair, and Sarah Pearl.

Mortality of newborn infants in Chicago during 1935, with special reference to the premature. H. N. Bundesen, O. A. Dahms, W. I. Fishbein, and G. E. Harmon.
Migrating Grafenberg contraception ring. C. J. Andrews.
A clinical study of abortion. (Editorial).

Vol. cvii, No. 5, August 1st, 1936.
*Heart disease and pregnancy. Julius Jensen.

Vol. cvii, No. 6, August 8th, 1936.
Contact dermatitis from menstrual pad. Frank E. Cormia.
The Chicago city-wide plan for the care of premature infants. Julius H. Hess.

Vol. cvii, No. 8, August 22nd, 1936.
*The blood changes in normal pregnancy and their relation to the iron and protein supplied by the diet. Frank H. Bethell and Ann Arbor.

Vol. cvii, No. 9, August 29th, 1936.
Experimental production of malignant growths in mice by oestrogenic chemicals. William U. Gardner, George M. Smith, Leonell C. Strong, and Edgar Allen.

Vol. cvii, No. 10, September 5th, 1936.
Milk not potent for cevitamic acid. (Editorial).

HEART DISEASE AND PREGNANCY.

Everybody agrees that the cardiac work is increased during pregnancy, and the author suggests that this is due mainly to the larger minute-volume output of the heart. Analysing a series of pregnancies associated with cardiac disease, he found that the mortality was 5.8 per cent, and that the greatest single cause of death was congestive failure. Apart from this he found that the death-rate from pneumonia, embolism, pulmonary infarction, and sepsis was greatly increased in patients suffering from cardiac disease, whereas the death-rate from renal disease and eclampsia was not affected by this complication.

It was found that the commonest times for death to occur were during, and immediately after, labour. After this the death-rate fell until the second week of the puerperium, at which time the patient might succumb to pulmonary lesions. The mortality-rate of those patients who died undelivered rose with the duration of the pregnancy until the twenty-eighth week, after which it was usual for delivery to precede death.

In all cases the prognosis is most influenced by the functional state of the cardio-vascular system. Of the various valvular lesions the combination of mitral and aortic lesions carried by far the highest death-rate, while the presence of auricular fibrillation was of grave import.

The author believes that the widely held idea that pregnancy shortens the lives of women suffering from cardiac disease has yet to be proved, and states that there is no evidence that the age of death is less among parous women. The evil effects of pregnancy on cardiac disease seem chiefly to be that it may precipitate congestive failure, when this is imminent, and aggravate it when it is present.

THE BLOOD CHANGES IN NORMAL PREGNANCY AND THEIR RELATION TO THE IRON AND PROTEIN SUPPLIED BY THE DIET.

With a view to estimating the blood changes in uncomplicated pregnancies, blood tests were made on an unselected series of gravid women at intervals during the last 13 weeks of gestation, healthy nonpregnant women being used as controls. In the control group the average haemoglobin was 87.5 per cent. The authors believe that the hydraemia occurring in pregnancy may cause this figure to fall as low as 70 per cent, but in the present series values below this were found in 70 per cent of the pregnant women, and these were considered to be suffering from pathological anaemia. These anaemias fell into two groups. The first type was characterized by low colour index, small red blood-cells and an increased percentage of reticulocytes. In this type the bone marrow is reactive and its normoblast content is greater than in the non-anaemic person. The condition is due to lack of iron. But the condition rapidly responds to the administration of inorganic iron in adequate doses. The second type of case was characterized by an approximate equivalent reduction in red blood-cells and haemoglobin, resulting in a colour index of near unity, by a normal or increased size of erythrocytes, and by a reticulocyte percentage below the average normal range. In these cases the bone marrow is relatively inactive with little evidence of regeneration. The authors regard this type of anaemia as being due mainly to deficient intake of protein of high biological value, and obtained good results from giving high protein diets. In conclusion, the routine administration of iron is advocated during pregnancy, together with a diet containing an adequate amount of protein.

F. H. Finlaison.

Gynécologie et Obstétrique

Vol. xxxiii, No. 6, June 1936.

A study of accidental haemorrhage. Fruhinsholz and Petroff.

The value of blood transfusion in gynaecology. Goudim-Leknovitsch.

A case of quadruplets. Dobis.

*The significance of the implantation of an embryo on the summit of a tubal plica: the so-called columnar implantation. Hoffmann.

Extraperitoneal Caesarean section in infected cases. Ramos and Bello.

The value of microscopic examination of the contents of artificially produced vesicles in cases of puerperal infection. Iljine.

Vol. xxxiv, No. 1, July 1936.

*Metaplastic and hyperplastic lesions of the cervix. Laffont, Montpellier, Laffargue.

The medicinal control of labour in cases of tardy dilatation of the cervix. Kreis.

A case of a fibro-adenoma extruded during the puerperium. Danen and de Watteville.

Cases of extra-uterine gestation. de Sa.

Eclampsia in Ousbekistan. Tchertock.

Vol. xxxiv, No. 2, August 1936.

The pathogenesis of pernicious vomiting of pregnancy. Voron and Pigeaud.
A comparison between uraemic and eclamptic convulsions in pregnancy. Chappaz.
*Diathermy as an initial step in a therapeutic abortion. Tsoutsoulkovskaya.
The treatment of eclampsia with magnesium sulphate. Browkin.
An abscess of the parametrium bursting into both the uterus and the rectum. Geisendorf.

THE SIGNIFICANCE OF THE IMPLANTATION OF THE EMBRYO ON THE SUMMIT OF A TUBAL PLICA: THE SO-CALLED COLUMNAR IMPLANTATION.

Hoffmann describes three cases of tubal gestation in which at operation a superficial inspection of the Fallopian tubes revealed no abnormality despite much free blood in the peritoneal cavity. Further inspection, however, of the Fallopian tubes, after all other possible sources of bleeding had been excluded, revealed some slight dilatation of one tube, which was then removed.

In each case the embryo was found to be implanted on the summit of one of the ampullary plicae, forming, as it were, a tubal polyp. The absence of the invasion of the muscular wall, which occurs when the implantation site lies between two adjacent plicae, explains why the outside of the tube appears normal in such cases. The readiness with which complete separation of the ovum occurs in columnar implantations explains why serious symptoms develop suddenly and without warning at an early stage of pregnancy.

METAPLASTIC AND HYPERPLASTIC LESIONS OF THE CERVIX.

The authors maintain that true leucoplakia is distinguished from simple hyperplasia by the presence of a stratum granulosum containing eleidin and keratohyaline granules. They denote as pre-leucoplakia a condition in which, although no stratum granulosum can be seen, the superficial layers of the rete mucosum have become flattened and stretched. Such an appearance is common at the edge of patches of true leucoplakia. Pseudo-leucoplakia is a condition of simple hyperplasia in which, while no keratinization has occurred and the cells remain clear, the superficial cells partially desquamate and, taking up eosin readily, simulate a horny layer.

After discussing the various opinions expressed by other workers on the question of whether these various lesions are pre-cancerous, they conclude that simple epithelial hyperplasia is not pre-cancerous and is a terminal or regressive lesion. True leucoplakia must be regarded as pre-cancerous on the analogy of other mucous surfaces, notably the buccal mucosa, but no exact figures of the chances of subsequent malignant change can be given as some authors claim to be able to do.

DIATHERMY AS AN INITIAL STEP IN THERAPEUTIC ABORTION.

The author finds that pelvic diathermy administered an hour or more before the performance of therapeutic abortion not only softens the cervical canal, rendering the operation more easy, but also reduces the incidence of pyrexia. A fuller advantage claimed for pre-operative diathermy is a definite anaesthetic effect upon the cervix.

She uses a current of one ampere, applied by means of a smooth vaginal electrode touching the posterior fornix and a suprapubic electrode with a surface of 150 to 250 square centimetres. The duration of each treatment varies between 15 minutes and one hour.

P. Malpas.

Bulletin de la Société d'Obstetrique et de Gynécologie de Paris, Etc.

Vol. xxv, No. 6, June 1936.

SOCIETE D'OBSTETRIQUE ET DE GYNECOLOGIE DE PARIS.

*An abdominal belt for use in the second stage of labour. Léon and Ferrari.

*Follicle development in vulval ovarian grafts induced by the injection of hormones extracted from urine. Moricard.

*Development of the genital tract and menstruation following the injection of dihydrofolliculin benzoate. Moricard.

*Mammary and pigmentary changes occurring in a girl after treatment with folliculin for gonorrhoeal vulvitis. Moricard.

Luteal haemorrhages due to disturbed anterior pituitary function. Moricard and Palmer.

A speculum transparent to X-rays. Lévy.

A uterus subseptus. Cleisz.

A rare genital tumour. Le Lorier, Isidor, and Maricot.

*The dangers of lipiodol injection into the Fallopian tubes and peritoneal cavity. Béclère.

An ossified cephalhaematoma. Digonnet.

SOCIETE D'OBSTETRIQUE ET DE GYNECOLOGIE D'ALGER.

*Congenital spondylolisthesis. Laffont and Fulconis.

Four cases of Le Fort's operation in old women. Vergoz and Choussat.

Caesarean section for an intramural cervical fibroid. Laffont and Ezes.

A lower-segment Caesarean section for a breech presentation in a fibroid uterus. Laffont and Ezes.

Death following hysterectomy for accidental haemorrhage. Laffont and Schebat.

Lower-segment Caesarean section for acute pulmonary oedema. Ezes and Schebat.

Serum therapy in the puerperium. Schebat and Coriat.

SOCIETE D'OBSTETRIQUE ET DE GYNECOLOGIE DE LYON.

*A case of intra-uterine foetal melaena. Brochier and Magnan.

Forty cases of placenta praevia treated by Caesarean section. Voron and others.

Multiple knots in the umbilical cord causing foetal death early in pregnancy. Voron and others.

Severe anaemia in pregnancy. Pigeaud and others.

A case of syphilitic osteochondritis in a newborn child: the so-called Parrot's palsy. Trillat and Cornut.

A tuberculous ulcer of the labium majus with death from miliary tuberculosis during the puerperium. Gonnet, Banssillon, and Joly.
The cardiac malformations of the newborn. Banssillon and Joly.
Three deaths during the puerperium. Rhenter and Burthiault.
A malignant leio-myoma. Villard, Caillot, and Contamin.

REUNION OBSTETRICALE ET GYNECOLOGIQUE DE NANCY.

A fibroid of the anterior lip of the cervix. Michel.
A rapidly growing sarcoma of the cervix. Binet and Devain.
Section of the internal pudic nerve in a case of intractable pruritus vulvae. Binet and Devain.
The after-history of a bleeder operated upon for peritoneal haemorrhage from a ruptured follicle. Guillemin.
A phantom ovarian tumour in pregnancy. Vermelin.

AN ABDOMINAL BELT FOR USE IN THE SECOND STAGE OF LABOUR.

The authors claim that the application and progressive tightening of an abdominal belt during the second stage materially shortens labour and reduces the number of forceps deliveries.

FOLLICLE DEVELOPMENT IN VULVAL GRAFTS INDUCED BY THE INJECTION OF URINARY EXTRACTS.

Moricard describes two cases of vulval grafts in which the injection of extracts of pregnancy urine induced follicle formation. In the first case distension of the follicle was obtained on two occasions by the injection of 120 mouse-units, and the fluid obtained by aspiration of the distended follicle induced vaginal keratinization in a mouse. In the second case, which is described in more detail, the injections were given over a period of 15 months, commencing five months after the insertion of the graft.

The dose required had to be progressively increased from 100 units to 400 units at the end of a year to obtain swelling of the graft and the production of follicular fluid. At the end of 15 months no further effects could be obtained.

DEVELOPMENT OF THE GENITAL TRACT AND MENSTRUATION FOLLOWING THE INJECTION OF DIHYDROFOLLICULIN BENZOATE.

Moricard describes the following cases illustrating the action of dihydrofolliculin benzoate.

1. A girl aged 26 years had both appendages removed for bilateral salpingitis. Cervical biopsy three months later revealed atrophy of the cervical mucosa, the cytoplasm and cervical glands appearing clear with Van Gieson's stain; she was given a dose of 20 milligrams of dihydrofolliculin benzoate in four doses spread over 14 days. Cervical biopsy practised immediately at the end of the treatment revealed hyperplasia of the cervical mucosa and a return to the normal intense staining of the cells with mucicarmin.

2. This patient was seen two months after the removal of both appendages, when she complained of severe menopausal symptoms. She was given 30 milligrams of the drug spread over a period of three weeks. At the end of

the treatment she had a slight vaginal loss. A biopsy was done immediately and she then had a loss lasting for six days. Six weeks later she was given a further 25 milligrams; this was immediately followed by a loss lasting four days. A third treatment with five milligrams was given the next month, followed by a slight loss immediately after the treatment. The main features of the endometrium after treatment were the absence of any signs of secretion and marked proliferation and oedema of the stroma.

3. This patient had had bilateral oöphorectomy six months previously. She was given folliculin benzoate in a dosage of 45 milligrams for a period of 18 days, followed by 30 milligrams of lutein extract for a period of 10 days. At the end of the treatment she had a loss lasting for six hours. The outstanding clinical feature of the treatment was the resolution of a large cervical ulcer with its attendant purulent discharge.

MAMMARY AND PIGMENTARY CHANGES OCCURRING IN A GIRL AFTER TREATMENT WITH FOLLICULIN FOR GONORRHOEAL VULVITIS.

In one case the injection of six milligrams of folliculin benzoate for gonorrhoeal vulvitis caused immediate enlargement of the mammary glands lasting for three weeks. In the second case 13 milligrams were given over a period of 15 days. Marked enlargement of the breasts occurred, but no secretion appeared. The treatment was continued for two months, by which time the child had received 18 milligrams. The breasts diminished in size, but the areolae remained pigmented and Montgomery's tubercles remained prominent. A definite linea nigra appeared and persisted. The hymen became soft and its apperture larger.

THE DANGERS OF LIPIODOL INJECTION INTO THE FALLOPIAN TUBES AND PERITONEAL CAVITY.

Béclère discusses the complications of lipiodol injections. He concludes that the pelvic peritoneum is completely tolerant even in cases of chronic pelvic infection. There is a slight risk attending the presence of lipiodol in the Fallopian tubes when cystic salpingitis is present. Four per cent to six per cent of these cases develop an inflammatory reaction. He adviseed restriction of the amount injected in cases in which salpingitis is suspected.

CONGENITAL SPONDYLOLISTHESIS.

Laffont and Fulconis describe in great detail a case of congenital spondylolisthesis. The main features of their were almost the complete disappearance of the fifth lumbar vertebra, forward displacement of the lumbar spine on the sacrum, acute anteversion of the lumbar spine, which became almost horizontal, with compensatory dorso-lumbar kyphosis, and lastly an almost vertical position of the sacrum.

A CASE OF INTRA-UTERINE FOETAL MELAENA.

At the end of a twin pregnancy the liquor amnii leaked for some days. It was noticed to be blood-stained, and it was thought that one of the foetûs was macerated. Both children, however, were born alive, and the first child was found to have melaena immediately after delivery, and for the three subsequent days. The author refers to four similar cases recorded in the literature.

P. Malpas.

Bruxelles Médical.

Vol. xvi, No. 36, July 5th, 1936.

*The cause of the onset of labour at term. C. van Bogaert.

Vol. xvi, No. 37, July 12th, 1936.

*The use of sodium evipan in obstetrics. van Boven.

Société Belge de Dermatologie et de Syphiligraphie. Report of proceedings.

Esthiomene of vulva due to soft chancre. M. Lapière.

Vol. xvi, No. 40, August 2nd, 1936.

*Breech delivery in a patient with a double vagina. M. Brouha and R. Bastin.

Academie Royale de Médicine. Report of proceedings.

The influence of the gonads on hypophyseal transplants in white rats. Mm. Deselin and Grégoire.

Société Medico-Chirurgicale du Brabant. Report of proceedings.

Aetiology and treatment of puerperal pre-eclamptic and eclamptic states. J. A. Schockaert.

Vol. xvi, No. 41, August 9th, 1936.

Nicolas-Favre disease. Benign suppurative peri-adenitis or peri-adeno-lymphangitis. Subacute inguinal lympho-granulomatosis of genital or venereal origin. Joseph Nicolas.

*Two cases of primary carcinoma of the female urethra treated by irradiation. Paul Desaive.

*Dystocia due to a foetal monster. M. Brouha and A. Wery.

Vol. xvi, No. 42, August 16th, 1936.

Nicolas-Favre disease (continued). Joseph Nicolas.

*Remarks on the use of evipan in obstetrics. A. Verdonk.

Vol. xvi, No. 43, August 23rd, 1936.

*Ovarian sarcoma complicating pregnancy and the puerperium. R. Schockaert.

THE CAUSE OF THE ONSET OF LABOUR AT TERM.

An historical survey of ideas on this subject commences with the views of Hippocrates, but deals in detail with the theories and experiments of the present century.

Possible foetal causes such as lack of nutrition, specific foetal products, alterations in the calibre of the umbilical vessels are all reviewed.

Among maternal theories are mentioned renal or hepatic insufficiency, changes in the colloidal state of the blood, alterations in the concentration of sodium and magnesium ions, and the sensitivity of the nervous system.

The author favours the suggestion that mechanical stimulation of the paracervical ganglia by the presenting part as being a possible mechanism.

The greater part of the article is devoted to a discussion of modern experiments and ideas concerning the endocrine control of pregnancy. The opposite effects of the corpus luteum and oestrogenic hormones are stated, and the role of the posterior pituitary and suprarenal hormones mentioned. The latter is considered to be oxytocic in the human subject.

Finally, the placenta, as the site of production of hormones, not only

gonadotropic and oestrogenic, but also specific, is invoked as an agent in the onset of parturition.

However, the author openly states that he draws no definite conclusions from this wealth of contradictory experimental evidence, and that the cause of the onset of labour is unknown.

THE USE OF SODIUM EVIPAN IN OBSTETRICS.

Some of the disadvantages of chloroform anaesthesia, such as difficulty in induction, mental trauma, delay in induction, pulmonary complications, led to a trial of evipan as an anaesthetic in obstetric practice.

Having had experience of 150 cases in which no maternal or foetal complications were experienced, the author concluded that this form of intravenous anaesthesia is excellent. The application of forceps, version, manual removal of the placenta, perineorrhaphy and Caesarean section were all carried out with the patient anaesthetized with evipan. The changes in the pulse-rate and blood-pressure throughout anaesthesia are recorded. Vomiting and headache are very rare sequelae. Evipan anaesthesia was used in patients suffering from pre-eclampsia without ill-effect. It induces good relaxation of the uterus.

It is difficult to estimate the required dose of evipan but sympathicotonic patients require more than do vagotonic patients. In this series the dose of one gramme in 10 cubic centimetres of water was not exceeded.

BREECH DELIVERY IN A PATIENT WITH A DOUBLE VAGINA.

The case recorded is one in which a woman of 39 years of age with two narrow vaginae conceived by vulval insemination. Pregnancy was normal except for mild toxaemia and the child presented by the breech. In labour a foot presented through the cervix in the left vagina. In spite of episiotomy, the delivery of the arms was difficult, and the child, weighing 3,000 grammes, lived for only ten hours. Manual exploration for the removal of the placenta revealed no abnormality of the uterine cavity.

The authors comment that breech presentations are unusually common in patients with double vaginae and believe that, although the child was lost, vaginal delivery was preferable in this case since the uterus is now without a scar, and one vagina is now sufficiently dilated to allow coitus.

TWO CASES OF PRIMARY CARCINOMA OF THE FEMALE URETHRA TREATED BY IRRADIATION.

One hundred and fifty-two cases of this disease have already been recorded. In the first of the two patients here described, carcinoma cervicis had been treated with radium four years previously. The urethral growth, however, was not a metastasis. It was treated, after biopsy, with interstitial radium needles and a radium plaque. The patient showed no evidence of recurrence four years later. The second patient had been treated for pruritus with deep X-rays when a small urethral tumour appeared. It was excised and was then found to be a carcinoma. Radium needles were inserted and the patient was well one year later.

In both cases the growth was early and was situated at the lower end of the urethra.

The clinical features such as multiparity, local irritation, and urethral bleeding are described. Pain is a late feature of the disease. The inguinal glands become involved in 33 per cent of the cases.

The various forms of treatment are discussed, and the author favours local treatment with radium followed by excision of glands if they are affected.

Dystocia due to a Foetal Monster.

Labour began prematurely in a multiparous woman suffering from hydramnios. A small child was delivered with the forceps but was still-born. Although there was obviously another child *in utero*, labour did not progress. Manual exploration revealed a deformed limb. An acardiac monster was delivered with some difficulty after embryotomy. The patient was severely shocked and manual removal of the placenta was required. The puerperium was uneventful.

Examination of the first twin revealed a cardiac abnormality. The acardiac monster had a well-developed trunk and lower limbs, but no head or arms.

Remarks on the Use of Evipan in Obstetrics.

Evipan anaesthesia is extremely useful in obstetrics and can be employed for Caesarean section as well as for minor and shorter operations. It is a pleasant form of anaesthesia which eliminates shock, vomiting and malaise.

Attempts to use evipan as an analgesic in normal labour failed since it was found impossible to regulate the dose so as to relieve pain without interfering with the uterine contractions.

Since the drug is destroyed in the liver, it should not be used in patients suffering from toxaemia of pregnancy, nor in those *in extremis*. The simultaneous administration of glucose may, by diverting hepatic activity, delay the destruction of evipan, and hence prolong the duration of anaesthesia.

Ovarian Sarcoma Complicating Pregnancy and the Puerperium.

Sarcoma of the ovary is not common and, in Schockaert's experience, usually occurs in young subjects. As a complication of pregnancy such tumours are extremely rare. Two cases are described. In the first case, two nodular tumours were noticed during pregnancy and labour, but were thought to be fibromyomata. It was not until five months later that the patient consented to operation: by this time ascites had developed and the tumours had enlarged considerably. Total hysterectomy was performed for bilateral spindle-celled sarcoma of the ovary. The ascites quickly recurred after operation and the patient left hospital in a dying condition.

The second patient experienced abdominal pain immediately after a normal delivery. This was at first thought to be due either to hydronephrosis or to torsion of the pedicle of an ovarian tumour. At operation a round-cell sarcoma of the left ovary was removed: the acute symptoms were due to rupture of lutein cysts which were found on the surface. The patient was well six months later.

The time of origin of these tumours is discussed, and the conclusion

reached that in both cases the ovarian lesion was probably present prior to conception. The author concludes by emphasizing the necessity of removing, as soon as possible, ovarian tumours noticed in pregnancy. Not only may they undergo malignant change, but they are liable to other complications such as torsion.

T. N. A. Jeffcoate.

Zentralblatt für Gynakologie

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*The recognition of disgerminoma ovarii. O. Frankl.
Tetany of hypophyso-genital origin with impossible delivery and Caesarean section. F. Wolff.
Prophylactic measurement of the bony pelvis in gynaecological laparotomy. R. Knebel.
Heterotopic decidual reaction in the portio vaginalis uteri. J. Ostrcil, jr.
A case of umbilical haematoma. R. Freisfeld.
*Findings with eunarcon. O. Gandow.

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*Kraurosis fornicis vaginae. A. Labhardt.
Approximate frequency of atypical epithelium of the portio. H. Hinselmann.
Carcinoma of the thymus during pregnancy. H. Kahr.
A new instrument for evacuating deep abscesses, especially in the pouch of Douglas; coagulation canula. W. T. Wiemer.
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Lymphangioma the size of a foetal head on the neck of a foetus extracted with the forceps and treated by operation. G. Szerb.

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Fibular defect and tibial fracture in the newborn. P. Caffier.
*Mastitis neonatorum and its sequelae. H. Kolbow.
Mud treatment of membranous dysmenorrhoea. E. Weiss.
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Unexpected action of prontosil upon unstriped muscular organs. E. Schneider.
Abdominal exploratory incision of the uterine fundus to elucidate the diagnosis between myoma and pregnancy. E. G. Abraham.

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*Studies in the transport of the ovum in the human being. I.—The separation mechanism of the ovum. P. Caffier.
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Post-operative parotitis. H. Steinmetz.
The treatment of post-operative gastric atony by continuous drainage. O. Iseli.
*Sterilization by high cervical amputation. J. Novak.

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Short-wave therapy in gynaecology. P. H. Schumacher.

*Hormonal determination of sex differentiation. F. Ludwig and J. v. Ries.

Further enquiry into pregnancy reaction in autoplastic grafts of rabbit's ovary into the anterior chamber of the eye. H. Dworzak and K. Podleschka.

Haemolytic jaundice and pregnancy. H. J. Freyschmidt.

Whether icterus neonatorum is avoidable? A. L. Scherbak.

Abnormally short umbilical cord and foetal malformations. H. Ruhl.

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The quinine and calcium treatment of abortion and uterine inertia. W. Henkel.

The grip in difficult delivery of the shoulder in breech presentation. F. A. Wahl.

Pathological pregnancy and haematopoiesis. M. A. Daniachij.

Placenta duplex and velamentous insertion of the cord. K. Podleschka.

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Esthiomene of the vulva as a result of a fourth venereal disease. H. O. Kleine.

Results of the fight against cancer. J. Beaufays.

The possibility of error in the radiological diagnosis of fracture of the humerus in the newborn. F. A. Wahl.

The treatment of menstrual disturbances with diathermy of the uterine mucosa. B. S. ten Berge.

Fever and menstrual cycle. E. Menninger-Lerchenthal.

*Whether there is a physiological sterile period in women? R. Araya.

Twelve years' experience of tubal insufflation with his own apparatus. R. Budimlic.

No. 36, September 5th, 1936.

Is intra-abdominal cervical Caesarean section credited to the Doerfler technique? H. R. Schmidt and v. Elmendorff.

Whether delivery by Caesarean section by the Doerfler method is an improvement on the long-used section findings? H. Rossenbeck.

Caesarean section for traumatic osteomyelitis of the pelvic bones with suppurating vaginal and perineal fistulae. A. J. Petschenko.

*A mishap after attempted sterilization by knotting of the Fallopian tubes; the need for curettage at the time of sterilization. P. Esch.

Gamma radiation erythema and its useful employment. St. Simon.

*Primary amenorrhoea. B. S. Ten Berge.

*Superficial embedding of the ovum in the ovary. A. Baidin.

Unilateral absence of the adnexa. A. Peters.

No. 37, September 12th, 1936.

The significance of the law of strain in the mechanism of the first stage of labour. K. de Snoo.

*Transillumination as a method of physical examination and its value in gynaecology. E. Klaften.

Our former results with eugenic sterilization. A. Wieszmann.

Three atypical forms of ageing uterine mucosa, leading to haemorrhage. R. Joachimovits.

Monster with ectopia abdominis, diaphragmatic hernia, and absent lower extremities. T. Koppany.

The Recognition of Disgerminoma Ovarii.

Frankl refers to the recent interest taken in disgerminoma ovarii. Up to the year 1935 only 64 cases had been recorded, whereas since that time numerous cases have been described. The relative frequency of these tumours may be estimated if an investigation undertaken by Klaften is taken as a standard. Out of 188 malignant ovarian tumours, 19 were granulosa-cell tumours and six were disgerminoma-cell tumours.

He refers shortly to two cases, which have occurred recently, under the care of Professor Hiess in Klagenfurt and Doz Antoine in Vienna, respectively. The first case was that of a single woman of 28 years, who had never menstruated and who had only rudimentary internal genital organs; the other was a nullipara of 31 years, with no previously recognized genital abnormality. Both gave a history of sudden onset with pain in the lower abdomen and vesical symptoms two and three weeks before operation. At operation in each case the pelvis was found to be filled by a solid non-adherent ovarian tumour of the size of a foetal head. In the first case the rudimentary uterus was removed with the tumour, but the other ovary could not be identified; in the second case the apparently normal uterus and the other ovary, after a diagnostic incision and suture, were left behind.

Histological examination showed a typical appearance at all levels of both tumours. There was a poorly vascularized connective tissue base; in parts the connective tissue cells had well-marked nuclei, and in others these were markedly poorly shown. Numerous islands and rods of round cells, as well as undifferentiated protoplasm, with very large deeply stained dark-blue nuclei, could be seen in this field. In other parts of the section there were small groups of similar cells, and even single isolated cells of the same type. Mitotic changes were frequent. There was a relatively large number of giant cells.

Findings with Eunarcon.

Gandow records his results with the use of eunarcon, either as a basal narcotic for big operations, or as an anaesthetic for smaller procedures. In all he has used it on more than 300 occasions with satisfactory results. He has found that for gynaecological operations a preliminary dose of opiate, such as pantopon-atrinal, is necessary and satisfactory. The narcosis by this means is deepened and prolonged. The administration should be slow and deliberate, especially in cases in which preliminary medication has been undertaken, with care to avoid depression of the respiratory centre. One cubic centimetre in 30 seconds seems to be a suitable rate for intravenous injection. Given to initiate narcosis, it can safely be followed by the inhalation of ether. In this case the quantity of ether used is definitely lessened.

When disturbances of respiration have occurred, chiefly as a result of want

of skill in administration, treatment with coramine or pituitrin combined with artificial respiraton has quickly been followed by the return of spontaneous respiration.

Eunarcon is especially useful for procedures which need only a short anaesthetic. Its advantages over evipan are that its action is less powerful and that it is more quickly broken down and eliminated, as well as being extremely simple to administer.

Kraurosis Fornicis Vaginae.

Labhardt describes shortly the history and clinical findings in six patients suffering from what he terms kraurosis of the vaginal fornix. The ages of the six patients ranged from 30 to 58 years. One patient was nulliparous, and the others had borne from one to five children each without any abnormality during pregnancy or labour. The oldest patient was 10 years past the menopause, and the other five showed signs of ovarian insufficiency with delayed menstruation. In addition the youngest patient was markedly adipose. The patients all sought medical help for identical symptoms, namely vaginal discharge with occasional bleeding of small degree and indefinite bearing-down pain, pain in the lower abdomen, and pain in the sacral region. On physiological examination all six women showed limitation of changes in the vaginal epithelium and deeper tissues to the vaginal fornices. Distal to this region the vaginal wall was in all respects normal.

Considering the pathogenesis of the condition, the writer points out that it is questionable whether the epithelial changes are secondary to the subjacent thickening or whether they are primary in origin. He himself is inclined to consider the change as starting in the deeper structures as an exaggeration of the normal changes which occur in the senile vagina with shrinkage of the vaginal vault.

In his cases there was not any history of any cause of the condition, such as operative delivery, inflammatory trouble, or foreign body in the vagina; neither could a definite date be given for the onset of the disease. In one case the patient was definitely menopausal and had definite leucoplakia of the vulva indicating some ovarian underfunction. The other five all had delayed menstruation.

On the assumption that the condition was associated with ovarian insufficiency, two of the cases have been treated by the administration of progynon. So far definite naked-eye improvement in the condition of the vaginal epithelium has followed treatment, while there has also been a return of menstruation. Whether the contraction of the deeper structures of the vaginal vault is also reversible is a question which will only be answered after a far longer course of treatment than has so far been possible.

Mastitis Neonatorum and its Sequelae.

Kolbow refers to the relative frequency of mammary engorgement in the foetus on the fourth to seventh day after birth. This engorgement occurs in male and female children alike, and is accompanied by the secretion of a bluish white fluid which is similar to the mother's colostrum. He explains this occurrence as being the result of the flooding of the foetal circulation with follicular hormone during the last weeks before term which sets up

glandular hyperplasia. At birth the supply is suddenly cut off, and what remains with the foetus is eliminated in the foetal urine by the fourth day of extra-uterine life. The sudden cutting off of the folliculin gives rise to the secretory phase of the already activated gland. During this stage if there is any trauma combined with the entrance of infective organisms along the widened ducts a definite mastitis can be set up, the intensity of which may be sufficiently great to lead to the formation of an abscess.

When definite mastitis has developed it must be treated along general surgical lines as though it had occurred in an adult patient. It must be remembered that in the female child it may be followed by the destruction of glandular tissue, and if an abscess has been opened the mammary ducts may be cut across and eventually lead to trouble during child-bearing life.

The writer describes such a case in full. The breast on one side was markedly smaller and situated on a higher level than that on the other side. During pregnancy there had been considerable pain from drag on the scars of the smaller breast, and, after lactation began, the output of this breast was so restricted that supplementary feeding had to be resorted to.

STUDIES IN THE TRANSPORT OF THE OVUM IN THE HUMAN BEING. I.—THE SEPARATION MECHANISM OF THE OVUM.

Caffier has taken the opportunity of performing laparotomy on women for such conditions as genital prolapse without inflammatory trouble, to observe the condition of the ovaries and Fallopian tubes shortly before rupture of the mature Graafian follicle. To ensure that the operation was performed at a likely time he carried out a series of such operations on the twelfth day from the first day of the last menstrual period and, furthermore, to ensure a ripe mature follicle he preceded his operation by four injections of prolan on the tenth and eleventh day, the total dose being 3,400 rat-units.

Under these conditions he found the Fallopian tube on one side to be more turgid than usual, so that it had some degree of erectility. As a result the fimbriae of the Fallopian tube were curled round one pole of the ovary and enveloped the mature Graafian follicle, which was just ready to rupture. Under these conditions rupture of the follicle would be directly followed by the squirting of the mature ovum with its surrounding follicular fluid into the abdominal ostium of the Fallopian tube.

The steering of the abdominal ostium towards one or other pole of the ovary appears to depend upon the activity of the muscular isthmus of the Fallopian tube, and for this to come into full play it is essential that the tube shall be freely movable and not tethered in any way except by the fimbria ovarica. It is obvious, if this is the case in all instances of ovulation followed by pregnancy, that operations to reopen a closed Fallopian tube for sterility must be accompanied by freeing of any adhesions which hamper the movements of the Fallopian tubes before a satisfactory result can be expected.

STERILIZATION BY HIGH CERVICAL AMPUTATION.

Novak, in a short communication, makes a reply to the article on this subject published in the *Zentralblatt für Gynäkologie*, Number 13, 1936. He points out that three years is too short a time of observation to state that

patients are permanently sterilized by a high amputation of the cervix, and he also draws attention to the failure of Zoefgen in his 24 reported cases to note the condition of the uterus, Fallopian tubes, and ovaries.

He himself has had cases in which high amputation of the cervix for persistent cervical infection with sterility has been followed by repeated conception and a marked tendency to abort before full time. For this reason he tries to leave some portion of the cervix behind when dealing with a woman of child-bearing age. He considers that Zoefgen should follow up his series of cases more fully as regards the presence of libido, conceptional ability, fixation of the uterus and Fallopian tubes from inflammatory adhesions, and the character of the genital secretion.

As he has for many years not carried out a high cervical amputation in women of child-bearing age Novak is unable to furnish any information on this subject from his own practice.

HORMONAL DETERMINATION OF SEX DIFFERENTIATION.

Ludwig and Ries have carried out a series of experiments on incubating hens' eggs. On the fourth day of incubation they injected progynon into the allantois; the subsequently hatched chickens were found to be all hens. On repeating the experiment with the injection of androstin the chickens hatched were of both sexes in about equal numbers.

They point out that the standardization of progynon has been more accurately carried out than that of the male sex hormone and that, therefore, the dose injected was given with less certainty in the latter instance. They hope that when the male sex hormone is properly standardized to be able to produce male chicks, as they have already been able to produce female ones.

WHETHER THERE IS A PHYSIOLOGICAL STERILE PERIOD IN WOMEN?

Araya, after giving a short résumé of the statements of Ogino and Knaus with regard to the safe period in the woman's menstrual cycle, the records of other observers in connexion with pregnancy following a single coitus at different stages in the cycle, and pregnancy following artificial insemination, comes to the following conclusions: (1) The occurrence of a menstrual cycle lasting exactly 28 days occurs in only 40 per cent of investigated cases. In his own series of cases the proportion is even lower than this. (2) In any given woman the menstrual periods vary in duration and time of onset. (3) Ovulation can occur at any time during the intermenstrual period. (4) On the same grounds a corpus luteum may be found at any time in the intermenstrual interval. (5) Observations after removal of the corpus luteum at any time in the menstrual cycle have shown that the corpus luteum has no effect on the next menstrual period nor upon the contractility of the uterine musculature as described by Knaus. (6) The lessened viscosity of the cervical secretion, as described by Devraigne, Seguy, and Brandwein, can occur at any time in the menstrual cycle. (7) The occurrence of a pregravid condition of the uterine mucosa for the embedding of the ovum is not indispensable. (8) An examination of women, who in the course of a menstrual cycle have carried out only a single coitus, proves that fertilization is possible at all times and even during menstruation. (9) Pregnancy has resulted at any time in the menstrual cycle following artificial insemination. (10) The viability of the spermatozoa in the female genital tract is great enough to

render it possible for fertilization of the subsequently matured ovum to occur. (11) The viability of the ovum is at present unknown to us, but it appears to be at least two or three days in duration.

As a result of these conclusions the writer does not consider that the existence of a safe period in women has been established.

A Mishap after Attempted Sterilization by Knotting of the Fallopian Tubes; the Need for Curettage at the Time of Sterilization.

Esch describes the case of an epileptic patient who had been treated by knotting of both Fallopian tubes as a means of producing sterility. The operation was performed in March, and by the summer of the same year she was already suffering from amenorrhoea. In November of the same year she came under the writer's care with the object of having the pregnancy terminated and being adequately sterilized; she was then 14 weeks pregnant.

Laparotomy was performed and the uterus was emptied through a fundal incision, this incision being extended to include the intra-uterine portions of the Fallopian tubes, which were completely removed.

Examination of the removed Fallopian tubes showed that the left tube was not permeable to iodipin. The right tube could be filled from the ampulla; it was then demonstrated radiologically that it had become canalized from end to end. During the filling most of the serous adhesions on the surface gave way. The right Fallopian tube was so adherent to the ovary that this had been removed with it; the removed ovary contained a corpus luteum of pregnancy.

Knotting of the tubes as a method of sterilization is seldom practised. Mikulicz-Radecki performed this operation in only 11 out of 5,559 cases. It is also noteworthy that when the operation has been performed it was carried out by general surgeons and not by experienced gynaecologists.

This method is in no way to be recommended for legal sterilization under the present German law.

Primary Amenorrhoea.

Ten Berge points out that most cases of primary amenorrhoea result from defective ovarian function and that any uterine hypoplasia present is looked upon as being secondary to the ovarian condition. That this is not always the case is shown by von Tonkes, who states that there is a reciprocity between the uterus and ovary so that an ovary degenerates sooner when there is no functioning uterine mucosa. There are instances of non-menstruating women who become pregnant. Pregnancy may occur during lactation accompanied by amenorrhoea. Corpora lutea may be found in the ovaries after the climacteric.

It would seem that the uterine function is not, therefore, entirely dependent upon the state of the ovary. The uterus may be so underdeveloped that it is incapable of reacting to ovarian stimulation.

The writer quotes the case of a girl of 20 years of age who had never menstruated. The pelvis was explored during an operation for appendicitis. The uterus was small and infantile, the ovaries appeared normal, follicles were ripening in both ovaries, and in one ovary a normal corpus luteum was seen. The secondary sexual characteristics were well marked. Treat-

ment with folliculin over a period of three months was not successful in inducing menstruation in this case.

SUPERFICIAL EMBEDDING OF THE OVUM IN THE OVARY.

Baidin describes the case of an officer's wife, aged 32 years, who was married at 17 years of age and suffered from bilateral salpingitis at 22 years. Forty-two days after her last normal menstrual period she was operated on for extra-uterine pregnancy. The uterus contained two fibroids, which were enucleated, the Fallopian tubes were both intact, the left ovary was adherent to neighbouring parts and contained many cysts in its centre; this cystic portion was resected. The right ovary was densely adherent to the side of the uterus and enlarged, a bleeding mass of the size of a walnut projected from its free margin. The abdominal cavity contained one and a half litres of blood. The right ovary was freed and removed. An examination of the specimen showed it to consist of the entire right ovary containing a normal corpus luteum. Projecting from the surface of the ovary, and nowhere in contact with the corpus luteum, was a haematoma on the side nearer to the corpus luteum.

Serial sections of the whole specimens were made. The haematoma was enclosed in a capsule composed of connective tissue, blood-vessels and plasma cells. There were no luteal, follicular or chorionic elements in this capsule. Inside the capsule in the carneous mass chorionic villi were seen. In all sections there was a definite capsule of connective tissue separating the corpus luteum from the chorionic tissue.

This specimen would appear to be one of extra-uterine pregnancy in which the ovum has not been fertilized inside the Graafian follicle and developed there but has embedded itself on to the surface of the ovary after it had escaped from the follicle, the bleeding into the abdominal cavity had occurred from a rupture on its outer surface. The writer gives illustrations of the whole specimen, the specimen split into two, and drawings from reconstruction of numerous serial sections.

TRANSILLUMINATION AS A METHOD OF PHYSICAL EXAMINATION AND ITS VALUE IN GYNAECOLOGY.

Klaften refers to the penetration of light from the cystoscope in the distended bladder through the vesical wall across the abdominal cavity and up to the abdominal wall. With a good light and a thin patient he has on occasion been able to make out the outline of tumours in the abdomen and to decide whether they were solid or cystic in character.

As an improved modification he has devised an apparatus which may be used to transilluminate the abdomen with a light placed in the rectum or vagina. He terms this apparatus a cystodiaphanoscope.

In introducing an electric bulb into the rectum or vagina it is not separated from the wall of the viscus by the lotion surrounding it. While this makes for a greater intensity of illumination the heat produced may be very considerable and can give rise to rapid discomfort or even pain. For this reason he has had to use a very small bulb and switch on the light for very short periods at a time.

If these precautions are taken he considers that transillumination is of value in gynaecological diagnosis. R. H. B. Adamson.

Münchener Medizinische Wochenschrift

March 20th, 1936.

The use of the stereosthethescope in obstetrics. G. Duseberg.

March 27th, 1936.

*Appendicitis in pregnancy. C. Evelbauer.

*The conduct of labour in domestic practice, with early rupture of the membranes. Prof. Holtermann.

May 1st, 1936.

*Puerperal neuritis of traumatic origin. G. Gaehtgens.

May 8th, 1936.

*Accidental haemorrhage. E. Vogt.

May 15th, 1936.

Cardiozol-sugar infusion for the premature child. H. Nevinny.

May 22nd, 1936.

Birth injuries of the child. H. Naujoks.

*Induction of labour and the treatment of inertia by chinin-calcium. H. Winkler.

June 19th, 1936.

The generative glands and the hormonal sex system. L. Seitz.

June 26th, 1936.

Factors adversely affecting the foetus *in utero*. H. Naujoks.

The menstrual cycle of 21 days. H. Füth.

July 3rd, 1936.

*The treatment of puerperal fever with prontosil. L. Ley.

APPENDICITIS IN PREGNANCY.

An account is given of the clinical details, treatment, and results of nine cases of acute appendicitis during pregnancy. All were operated on and recovered. The author points out the importance and difficulty of early diagnosis, the difficulty increasing the longer the pregnancy. The sudden onset of abdominal pain and its later localization are stressed. In two of the cases there was coincident cystitis or pyelitis, and it is pointed out that the presence of a urinary infection does not exclude appendicitis being the real cause of the general condition. Early operation is advocated no matter the stage of the pregnancy, and the author remarks that it is better to exclude appendicitis by operation than to fail to diagnose the condition. An abscess should be drained. In regard to the uterine contents expectancy is advocated, and if interference is indicated the vaginal route is to be employed. In both cases when peritonitis was present abortion occurred. Uterine sedatives are advised during the post-operative period.

THE CONDUCT OF LABOUR IN DOMESTIC PRACTICE COMPLICATED BY EARLY RUPTURE OF THE MEMBRANES.

The author confines his remarks to cases of premature rupture of the membranes during the last four weeks of pregnancy. If labour does not begin spontaneously within a few hours he advocates the use of quinine or

thymophysin. In all cases it is necessary to exclude first of all any causal abnormality such as hydramnios, oblique lie, pelvic contraction, or twin pregnancy. Uncomplicated cases are to be examined as little as possible because of the danger of infection, and interference should be minimal. The author believes that intercourse during the latter part of pregnancy is responsible for some cases and that, therefore, advice should be given on this subject to patients.

PUERPERAL NEURITIS OF TRAUMATIC ORIGIN.

Two cases of marked peripheral nerve lesions in the legs have been observed by Dr. Gaehtgens during the puerperium. Both patients had been delivered operatively: in the first case perforation was performed, and in the second rotation of the occiput followed by delivery with the forceps. A few days after delivery the patients had severe pains in the legs, corresponding to a tibial nerve distribution, and marked paresis. There were not any abnormalities of the reflexes. The treatment adopted was the standard one of radiant heat, massage, and electrotherapy. Recovery occurred. The author also administered Baler's vitamin B preparation, betaxin, noticing rapid improvement after eight doses.

ACCIDENTAL HAEMORRHAGE.

Premature separation of the normally situated placenta is caused by two main factors. In the one the placenta is separated by some mechanical means such as trauma, abnormally short cord, operation, or induction; in the other there is a primary retro-placental haemorrhage. The author confines his paper to the latter group. The aetiology of these cases is still uncertain; it is his belief that albuminuria and signs of toxaemia are present in 90 per cent of cases. Konver and De Snoo found the incidence of retroplacental haemorrhage to be one in 22,000 normal pregnancies; one in 220 in cases of albuminuria, and one in 56 in cases of eclampsia. The latest theory is that an over-production of anterior pituitary hormones is the responsible agent. Heim has described nine such cases in which eight showed an increase in these hormones. The diagnosis between accidental haemorrhage, placenta praevia, and uterine rupture is discussed.

Treatment is now neither conservative nor radical, and each case is to be judged on its merits. Von Konver published a series of 78 cases treated by him with a maternal mortality of 11.5 per cent and a foetal mortality of 68 per cent. De Snoo by expectant treatment in 165 cases had a maternal death-rate of only five per cent and a foetal mortality of 78 per cent. It is now the teaching in Vienna that the more radical methods do not improve the results. Blood transfusion, aided by saline and glucose, is stressed as being of most value. Pituitary preparations injected by all routes, including injection into the uterine wall, are most important. The author considers that prophylaxis is possible to some extent in that the detection and treatment of pre-eclampsia and syphilis will help.

INDUCTION OF LABOUR AND THE TREATMENT OF INERTIA BY CHININ-CALCIUM.

The clinical observations of a trial of a sandoz preparation of quinine and calcium, extending over two and a half years, are summarized. The

preparation has been used to start labour, in cases of primary inertia with and without associated early rupture of the membranes, and in cases of secondary inertia. Usually two injections of seven or nine cubic centimetres were given intramuscularly at an interval of an hour. In cases without contractions 77 per cent responded to the injection if they were in the last month of pregnancy. All patients with primary inertia seemed to be benefited; 44 out of 51 with early rupture of the membranes responded; in patients with primary inertia only and intact membranes 48 patients (27 primiparae and 21 multiparae) improved. Of the primiparae 25 were delivered within 12 to 14 hours; in multiparae delivery occurred in 40 minutes. Good results were not obtained in patients with secondary inertia.

THE TREATMENT OF PUERPERAL FEVER WITH PRONTOSIL.

The author has been very satisfied with results obtained from the use of this Bayer preparation in cases of puerperal infection. It can be given intramuscularly or by the mouth and doses of about 40 cubic centimetres daily are advised. No explanation is advanced as to the method by which it works, but the leucocytosis is not increased. Prophylactically used in suspect cases (42), 35 remained free from fever; 37 cases of actual infection were treated with good results in 28. The author considers that if given within the first 48 hours of infection it definitely influences the extent of the process.

K. Bowes.

The Medical Journal of the Netherland Indies.

*The frequency of syphilis among Chinese women of the average well-to-do class in Batavia.

THE FREQUENCY OF SYPHILIS AMONG CHINESE WOMEN OF THE AVERAGE WELL-TO-DO CLASS IN BATAVIA.

An obstetric-anamnestic, serological, and cursory clinical investigation of 841 pregnant Chinese women, who from May 1931 till June 1935 attended the Jang Seng Ie Maternity Centre at Batavia, which investigation was also, in doubtful cases, extended to the husbands, revealed a minimal frequency of syphilis of rather more than 7.5 per cent. This figure approximately corresponds to that found in various maternity centres in Europe. The prevalent opinion that the Chinese group of the population of this country should be strongly tainted with syphilis, needs drastic revision.

The frequency of albuminuria among the Chinese women under discussion is rather more than three per cent. This figure is much lower than that of pregnant women in Europe, where a maximal frequency of 20 per cent has been reported.

The above conjointly warrant the conclusion that the medical supervision in a maternity centre for Chinese women should be primarily directed to the detection of syphilis.

For the detection of syphilis in pregnant women systematic blood-tests are necessary. The Wassermann reaction, both in the case of a positive and of a negative result, in the case of pregnant women, should be accepted only with certain restriction.

The number of unspecific Wassermann reactions among pregnant Chinese women is about 0.5 per cent, a much lower figure than has been found among pregnant women in Europe.

For a better diagnosis of syphilis in pregnant women and an efficient combating of hereditary syphilis a close co-operation is necessary between maternity centres and infant welfare centres.

Archivo de Ostetricia e Ginecologia, Lisbon.

Vol. i, No. 1, December 1933.

Discourses at the inauguration of the Alfred da Costa Maternity Hospital. Monjardino, Costa, and Sacadura.

Account of visits in June 1933 to study maternity and infants' protection hospitals, especially in Italy.

Clinical reunions at the Alfred da Costa Maternity Hospital.

Vol. i, No. 2, April 1934.

*A rare case of foetal monstrosity. Sacadura, De Campos, and Horta.

*Haematometra and haematosalpinx. Monjardino.

Parturition in narrow pelves and the test of labour. Cabral and Sacadura.

Dimorphism of epithelial tumours of the cervix. A case of secondary dimorphism. Da Silva and Horta.

*Disjunction of the pubic symphysis during the application of the forceps. Cabral and Sacadura.

A case of atresia of the vagina. Leite.

History of Portuguese obstetrics in the seventeenth and eighteenth centuries. Costa and Sacadura.

Vol. ii, No. 1, April 1936.

An account of visits to France, Germany and Switzerland. Sacadura, De Campos, and De Sampaio.

*A study of blood-groups in newly born and suckling children. De Sousa.

*Biological methods in the diagnosis of pregnancy. Mendes and Leite

Travel notes. Institutions of pathological anatomy visited from 1933 to 1935 in the United States of America. De Oliveira.

Obstetric radio-diagnosis. Coelho.

Visits to maternity and children's institutions in France and Belgium, 1935. Da Silva.

Course of medical myology under Professor Langeron and practical work in the laboratory of parasitology (Section of Myology), Faculty of Medicine, Paris. Leite.

The social role of the midwife. Costa and Sacadura.

A Case of Foetal Monstrosity.

The authors report a case of foetal monstrosity, interesting because of its relative rarity—one in 5,000 according to Stoeckel.

The mother, who was aged 29 years and had one child, was admitted to hospital at term in labour. The first diagnosis made was incomplete pelvic presentation of a live child. Later a foot presented with a prolapsed

and pulseless cord. An attempt to deliver the infant was frustrated by its hugely enlarged abdomen. After evacuation of over a litre of fluid, the liver and kidneys were felt to be enlarged. Embryotomy had to be performed. The macroscopic diagnosis of the child was micro-cephalic, meningo-cephalic, polydactylia, clubbing of the hands (seven fingers) and feet (six toes), cystic liver and cystic kidneys, absence of mammary and suprarenal glands.

There is no doubt that in teratological cases like this the endocrine glands, especially the suprarenal, hypophyseal, and thymus glands, are constantly modified. Various causes may provoke these changes—tuberculosis, syphilis, lead-poisoning, and alcoholism. In this case the syphilitic reaction of the mother was negative and the child showed no special syphilitic lesions. But the weight of the placenta, and the backward foetal development support the possibility of hereditary syphilis. A microcystic kidney also suggested hereditary spyhilis.

HAEMATOMETRA AND HAEMATOSALPINX.

Monjardino describes two cases of haematometra occurring in young women, aged 23 and 18 years respectively, who had never menstruated. In each case there was an accumulation of thick sanguineous fluid caused by obstruction of the outflow. In the first case there was an imperforate septum in the vagina, and in the second across the cervix. The diagnoses made were: (1) haematometra, haematocolpos due to vaginal atresia, (2) haematosalpinx. The liquid was clinically aseptic.

In the first case the vaginal septum was incised. In the second the uterus was amputated supravaginally preserving the right ovary. Both patients made good recoveries. Normal menstruation came on a few weeks after dismissal and continued regularly.

Monjardino discusses whether such cases of retention are congenital or acquired. In early adolescence they are probably congenital when there is no history of inflammatory lesions.

DISJUNCTION OF THE PUBIC SYMPHYSIS DUKING THE APPLICATION OF THE FORCEPS.

Sacadura describes a case of disjunction of the pubic symphysis during the application of forceps for eclampsia in a primipara aged 18 years; the pelvic measurements were normal. When the attack occurred an intravenous injection of magnesium sulphate was given and preparations were made for the application of the forceps. The cervix was fully dilated.

Under ether anaesthesia strong, but not violent, traction was made with the forceps. The head was progressing slowly when suddenly a crack was heard followed by a rebound of the head. Labour terminated with the birth of a live child with a normal head and no unusual forceps marking. At this moment vulval disjunction was noticed at the left ramus of the pubis and a separation about a finger's breadth at the symphysis. The vulva was replaced and the symphysis was sutured; the retropubic space was drained. The wound suppurated but eventually healed. When the patient was allowed to walk she was slightly lame and complained of pain in the inguinal region. X-ray examination showed there was still a gap of about a centimetre at the symphysis.

Disjunction of the pubic symphysis is not a very frequent occurrence.

Statistics of Brown and Fernwald in 1894 show only three cases out of 30,000 births (Keller). In a work studying eight cases during spontaneous labour, Keller arrives at the conclusion that it may take place (*a*) during engagement of the head in the superior strait when there is pelvi-cephalic disproportion, (*b*) during descent and rotation because of the raised pressure on a pubic ramus and the opposite sacro-iliac articulation, (*c*) in the inferior strait during disengagement in funnel-shaped pelves. The pubic rami are separated by the head and fracture the symphysis.

Factors in the accident are super-calcification of the head, weakness of the pubic ligaments and fragility of the symphysis possibly due to rickets or osteomalacia. The consequences are not always harmless, vesical complications and haemorrhage may supervene or septic infection of the joint, which may permanently affect the patient's ability to walk.

A Study of Blood-groups in Newly Born and Suckling Children.

The idea of blood-groups is relatively recent and is due to experimental work within the last 40 years. Transfusion used to be made between various species of animals, but accidents and failures were not attributed to the true cause—incompatibility of the blood.

In the middle of the nineteenth century Dumas, Landois and others recognized that this incompatibility in animals was due to the agglutinating power of serum for heterogeneous red blood-corpuscles. Managliani in 1899 observed an analgous phenomenon between human individuals though he did not appreciate its importance. In the same year Shattock read a paper on inter-agglutination in human beings to the Pathological Society of London. His observations made on patients led him to regard the process as pathological, and it subsequently became of diagnostic value in diseases, such as typhoid fever and tuberculosis.

The credit of recognizing that iso-agglutination was a normal phenomenon in human blood belongs to Landsteiner. Later he classified blood-groups into three types. Salazar gives tables of blood-groups according to Landsteiner, Jansky, Moss, Dungern-Hirzfeld and the League of Nations. The last classification has been adopted by himself in his determinations of Portuguese blood-groups in the mothers of children less than a year old (313 mothers, 190 newly born and 126 children under a year). In his technique he was careful to avoid any source of error. The identity of percentages in the differnet groups leads him to believe that a greater tendency to disease or death does not exist. At birth the newly born child had its own agglutinogens. Cases are rare in which differentiation occurs later; 35.6 per cent have their own agglutinins at birth. The formative activity of these rises till about the eighth month of life when there are 96.2 per cent. They have a double origin partly from the infant and partly from the mother across the placenta. In hetero-specific pregnancies there seems to be a mechanism of mutual protection between mother and child. The relation between hetero-specific pregnancy and the weight of the child, toxaemia of pregnancy and physiological jaundice of the newly born has not been verified. Blood transfusion has numerous indications, even in newly born and very young children; its use should be more widely extended. If a suitable donor cannot be found the mother's blood is almost certain to be compatible with that of her infant.

The study of blood-groups is the surest and most scientific method for determining paternity. Exceptions to Bernstein's law may be considered as strongly in favour, if not absolutely certain, in the determination of paternity. Portuguese legislation on this subject is still incomplete, but the importance of further investigations is recognized.

From an ethno-anthropological point of view Portugal belongs to Ottenberg's European type. Its biochemical index, either according to Hirzfeld's or Ottenberg's classification, has one of the highest values in Europe.

BIOLOGICAL METHODS FOR THE DIAGNOSIS OF PREGNANCY.

The authors give statistics of their results in the biological diagnosis of pregnancy at the Alfredo da Costa Maternity Hospital, Lisbon. The total number of tests made was 215. The methods used successively were the Aschheim Zondek reaction (55), Brouha's reaction, Hinglais's and Simmonet's test (39), and Friedmann's test (121 reactions). In the two first methods errors occurred probably due to faults of technique. The results of Friedmann's reaction were all accurate. It is the method of choice, being easy and rapid.

In cases of normal pregnancy a positive reaction was obtained as early as eight days after the first missed menstrual period. The results were variable in ectopic gestation. A negative result was of no value. A positive reaction depends on the presence of living chorionic epithelium. In cases of retention of pieces of the placenta the result depends on the same factor.

The formation of a placental polypus was accompanied by a negative biological reaction, but after malignant degeneration of these tissues the reaction was positive. The same took place with vesicular mole. A quantitative biological test can be used in the differential diagnosis between these conditions.

J. H. Filshill.

Boletin de la Sociedad de Obstetricia y Ginecologia de Buenos Aires

Vol. xv, No. 7, August 7th, 1936.

*Repeated symphysiotomy. Bazun and Caso.

*A case of eclampsia. Gravid glomerulo-nephritis? León.

Hysterectomy for suppurating myoma in the puerperium. Bazan and Biondini.

Vol. xv, No. 8, August 20th, 1936.

*A case of bleeding breast. Masciottra and Chilese.

*Wherloff's disease and follicular hormone. Masciottra.

Arrhenoblastoma of the ovary. Remote results. Ahumada and Calatroni.

Rupture of the uterus during parturition after previous Caesarean section. Ahumada and Calatroni.

REPEATED SYMPHYSIOTOMY.

The authors refer to the relative infrequency of a second operation of symphysiotomy in the same patient. Usually the pubic bones are sufficiently permanently separated to allow further spontaneous parturition.

The number of first cases in their hospital reached 200. In four cases the operation had to be repeated. In three cases the first operation had been followed by spontaneous deliveries. In one case there was an interval of eight years without pregnancy between the two operations.

Evidently the reasons for the second symphysiotomy were disproportion and uterine inertia.

A Case of Eclampsia. Gravid Glomerulo-nephritis ?

León describes a case of eclampsia in a primipara aged 21 years. The attacks began about the thirty-second week of pregnancy; the patient was admitted to hospital, after a series of fits, in a comatose state. There was not any history of renal disease previous to pregnancy. For about a month treatment with appropriate diet and medicine was carried out, but the eclamptic symptoms did not improve. Abdominal Caesarean section was performed; this was followed immediately by a disappearance of oedema, lowering of blood-pressure, and an increase in the quantity of urine excreted. Slight albuminuria persisted.

León discusses whether a true glomerulo-nephritis had arisen during pregnancy and not the usual glomerulo-nephrosis of eclampsia.

A relative abundance of blood-platelets of renal origin in the urinary sediment and a raised percentage of urea in the blood seem to indicate a glomerulo-nephritic process. The absence of albuminuric retinitis does not clear the diagnosis, since this complication may be observed in eclamptic glomerulo-nephrosis. Seitz insists that if, after delivery there is chronic nephritis and raised arterial tension, then during pregnancy there has been true nephritis. Though the renal manifestations cleared up in León's case, he thinks that during pregnancy the evidence was in favour of both inflammatory and degenerative lesions. The history and clinical examination of the patient excluded nephritis before pregnancy, and an incidental nephritic infection during pregnancy.

He concludes that the glomerulo-nephritis was the consequence of general and renal vaso-constriction due to toxaemia of pregnancy. Functional tests of the kidney helped to establish this diagnosis and also to explain the great improvement after delivery.

A Case of Bleeding Breast.

The authors describe a case of bleeding breast in a multipara aged 40 years. Three years before consulting them the patient had noted a painless, hard swelling in the lower and outer part of her right breast; blood-stained fluid began to ooze from the right nipple a few months later. The swelling had increased in size and the discharge continued.

On examination they found a number of ill-defined nodules in the right breast, radiating down and out like a rosary from the areola. The regional lymphatic glands were not enlarged and the skin was unchanged. The possibility of carcinoma suggested itself, because this is the cause of haemorrhage from the nipple in five to seven per cent of cases. The slow rate of growth, the absence of lymphatic enlargement, and the absence of cutaneous changes excluded cancer. The diagnosis made was intracanalicular papillomata. But taking into account the patient's age, and the

diffuse form with the recent increase in the size of the tumour, they decided to perform a simple amputation of the breast.

Microscopic examination showed a general and diffuse dilatation of three lactic ducts and their branches with multiple papillomatous formation. The glandular elements had atrophied and the stroma had undergone a diffuse hyaline change.

The authors think the operation was justified because the existence of such numerous small papillomata indicate the likelihood of malignant changes supervening.

WHERLOFF'S DISEASE (HAEMORRHAGIC PURPURA) AND FOLLICULAR HORMONE.

Wherloff in 1735 described a non-pyrexial haemorrhagic purpura and distinguished it from scurvy with which it had previously been confounded; he made a classification of purpuras according to their origin and symptoms.

The relation between haemorrhagic syndromes and ovarian disturbance had long been recognized as well as the connexion between the ovaries and haemophilia. The woman transmits the disease, but possesses something which immunizes her against it. This substance is probably of ovarian origin. Thomas and Birch obtained success in treating haemophilia with different preparations of ovarian extract. Ovarian changes seem to be predisposing or provoking causes of purpura. It is known that Wherloff's purpura occurs most frequently in women and is aggravated at the menstrual periods or only appears then. So-called vicarious, or complementary haemorrhages generally appear in patients with ovarian insufficiency.

Paola's patient, a widow aged 60 years, had the characteristic symptoms of Wherloff's disease in its chronic form. It began after the menopause, and had recently become serious. An attack of marsh fever 30 years earlier might have caused a predisposition to a haemorrhagic diathesis by causing splenic changes.

After treatment with intravenous calcium and extracts of liver had failed, splenectomy had been advised, but Planelles, of Madrid, counselled the administration of follicular hormones in large doses by the mouth.

The patient's condition immediately improved and remains good so long as she continues to take large doses of follicular hormone.

J. H. Filshill.

Revista de Gynecologia e d'Obstetricia Rio de Janeiro, Brazil.

August 1936

*Gangrene of the puerperal uterus Povoa.
*Total urethroplasty (Marion). Salgado.
Large pseudo-mucinous ovarian cysto-adenoma. Tostes
*Two cases of ectopic gestation. Reis.
Vulvo-vaginal myiasis. Furtado.

GANGRENE OF THE PUERPERAL UTERUS.

Povoa describes a case of uterine gangrene in a patient, aged 23 years with one child, recently under treatment in his maternity hospital at

Campos, Brazil. She was admitted on the fourth day of exhausting and ineffective labour, with a high temperature, foetid amniotic fluid, and a dead child; the head was arrested at the pelvic brim. During instrumental delivery the head separated from the trunk owing to extreme foetal maceration, and the cervix was badly torn. In spite of careful dressing and lavage, a septic discharge persisted for about a month. Fragments of necrotic uterine muscle came away in the discharge. Finally a piece about 15 centimetres long separated. She recovered after a stormy convalescence. It was subsequently noticed that the uterus had disappeared; it had, in fact, been discharged piecemeal in the lochia after undergoing gangrene.

Povoa reviews the literature of similar cases. He did not find any in the Agentine records. The first case published in Europe was that of Syromjatnikoff, in 1880; he thought the uterine infection was a complication of typhoid fever, as his patient had had that disease.

Beckman, in 1900, published 15 cases, mostly Russian, one of which had occurred before 1880. Beckman proved that the genital infection was not necessarily due to typhoid fever as the predominant septic organism was the streptococcus.

Povoa notes that his case resembles most of the others recorded, the patient being a primipara in prolonged labour, delivery being operative and the placenta removed manually. The chief complications to be dreaded are uterine and intestinal perforation leading to peritonitis, and metastatic pneumonia or pleurisy. Even too violent lavage may cause perforation of the uterus because of its friability.

Syromjatnikoff had called the disease "metritis dissecans". Povoa agrees with Beckman that "gangrena uteri puerperalis" is a more suitable and comprehensive designation.

Total Urethroplasty.

Salgado refers to lectures by Professor Marion, at the Society of Medicine and Surgery in Rio de Janeiro, on the subject of urinary incontinence in women due to urethral destruction, and on its treatment by plastic operations on the urethra.

Subsequently Salgado had occasion to apply this treatment in his own hospital at Gamboa to a patient 24 years old. A long and neglected labour had resulted in the loss of the anterior vaginal wall and the urethra. At first Salgado tried to reform the urethra by closing a recto-vaginal fistula and performing a plastic operation on the anterior vaginal wall. This operation was not successful. He, therefore, undertook a heteroplastic operation, using a strip of vagina from another patient operated on at the same time for cystocele. Urethral continence was thereby established; the capacity of the bladder after operation was 140 cubic centimetres. Some time after he performed a suprapubic cystotomy for a vesical calculus. At this operation he verified that the vesical orifice of the new urethra was formed by a double mucous fold. The patient's continence was doubtless due to this falciform fold.

Two Cases of Ectopic Gestation.

Reis describes two cases of ectopic gestation. (1) The first concerns a patient, in the second or third month of pregnancy, whose symptoms indi-

cated tubal rupture with great haemorrhage. Laparotomy was immediately performed. The right ovary and right Fallopian tube were swollen, cystic and inflamed. The left ovary was absent, the left Fallopian tube had ruptured and a haematocele was present in the pouch of Douglas. A second swelling occupied the place of the ovary; this was as large as a nut and united to the uterus by the ovarian ligament; it was not, apparently, connected with the tube. A tentative diagnosis of double pregnancy was made (*a*) tubal and (*b*) ovarian. Subsequent examination, however, evinced that the criteria of an ovarian pregnancy were not fulfilled.

The second case was that of a multipara aged 35 years, whose periods had been absent for 25 months. Before the ninth month foetal movements had not ceased, but the expected labour did not take place. The abdominal swelling remained and the patient came to hospital 16 months later. Examination showed a hard fixed tumour on the right side of the abdomen adherent to the uterus. The diagnosis lay between ectopic gestation and a fibroma of the broad ligament; operation was performed. It was found that the foetus occupied the whole of the right Fallopian tube which was unruptured.

Reis regards the case of interest because the pregnancy had reached the ninth month without rupture of the tube, and the dead foetus had remained there for 16 months without undergoing calcification; putrefaction had not taken place.

J. H. Filshill.

REPORTS OF SOCIETIES.

ROYAL SOCIETY OF MEDICINE.

At a meeting of the Obstetric Section of the Royal Society of Medicine held on Friday, June 19th, with Professor FLETCHER SHAW in the chair,

Mr. J. B. BLAIKLEY showed two specimens of

ANGULAR PREGNANCY.

The first specimen was from Mrs. R.S., primigravida, who was first seen by her doctor for a threatened abortion at the ninth week of pregnancy; further slight bleeding occurred at the twenty-second, twenty-third, twenty-sixth, and thirtieth weeks of pregnancy. Asymmetry of the uterus was noticed on every occasion, a prominent bulge being present on the left side; at no time during pregnancy was there any complaint of pain. At the thirty-sixth week of pregnancy she delivered herself spontaneously; there was no post-partum haemorrhage, but the placenta was retained, and it proved impossible to remove it manually; she was therefore admitted to Guy's Hospital, under Mr. Gibberd, who made a further exploration of the uterine cavity: he found it tightly contracted and it was impossible to define the placenta; a provisional diagnosis of placenta accreta was made and the uterus removed by subtotal hysterectomy. The specimen shows the placenta situated in what appears to be a thin-walled diverticulum in the left corner of the fundus, the wall of which is thin in this area, although elsewhere it has retracted and is of normal thickness. Sections show the decidua basalis is very imperfectly developed but is present, and that this is not a placenta accreta.

The second specimen was from a woman, aged 37 years, who had had eight normal pregnancies; in 1935 she again became pregnant, her last period being on July 27th. She was admitted to Woburn Hospital at the beginning of December for severe abdominal pain associated with slight uterine bleeding. Mr. Blaikley was asked if he would see her on December 12th, and he had her admitted to Guy's Hospital for observation. He kept her under observation for three weeks, and during the whole of that time she complained of constant pain with exacerbations so severe that a quarter of a grain of morphia did not relieve the pain. There was no vomiting. Examination always showed a very asymmetrical uterus which corresponded in size with her dates, but the enlargement was noticed to be mostly on the right side; further, the uterus was very tense and exceedingly tender to palpation at all times; there was slight haemorrhage almost every day in spite of rest in bed. X-ray showed a normal foetus, and the Friedmann test was positive in normal dilutions of urine. On January 2nd, Mr. Chapple saw the patient, and in view of the possibility of an interstitial pregnancy,

or, less likely, a fibroid undergoing necrobiosis, he decided to perform laparotomy. At operation the uterus showed marked asymmetry, and it was removed by subtotal hysterectomy. It was very striking how the patient's mentality and appearance changed after the operation, and it became additionally evident to him how severe had been the pain.

The specimen shows wide separation of the round ligament, the Fallopian tube and the ovarian ligament on the right side, but no separation at all on the left; the placenta covers the opening of the Fallopian tube, though its centre is behind this point.

It seemed that both these specimens should be described as angular pregnancies; the history of the first patient is atypical in the absence of pain, which was such a marked feature of the second. It seems likely that some abortions in which pain is a prominent feature both before and during the abortion are the result of angular pregnancies.

These specimens were discussed by Professor MUNRO KERR who mentioned points in the diagnosis and treatment of angular pregnancy.

Dr. STEWART WILSON presented a paper which, in his absence, was read by Mr. LESLIE WILLIAMS. The paper was entitled

TWO CASES OF FULL-TIME ECTOPIC PREGNANCY.

The first case was not seen by a qualified medical man until late in a labour which had been assisted by powerful abdominal pressure by native attendants. It is surmised that this pressure must have forced the child down into the pouch of Douglas, and at least partially to have ruptured the posterior vaginal fornix, and probably partly to have separated the uterus from its attachments, time then allowing clotting in the torn vessels. When the doctor examined the patient the head was tightly jammed in the region of the pelvic brim. He was able to push this up, get his hand into what he thought was the uterine cavity, do internal podalic version and deliver the child by the breech. Some difficulty was experienced with the head, which had to be extracted by the forceps, and it is the author's opinion that, but for the delay thus entailed, the child, which was only just dead, would have survived.

The placenta, however, would not come away, and eventually manual removal was attempted. The doctor doing this remarked to his assistant that he had never felt anything like it before, but continued his manual removal and eventually extracted the whole uterus. The placenta subsequently came away with traction on the cord, and though intestine now appeared down the much lacerated vagina, and though a few days later a recto-vaginal fistula appeared, the patient recovered. A few days later it was felt that exploratory laparotomy must be performed, and it was surprising that the upper abdomen was perfectly normal, while the pelvis was partly occupied by a mass about the size of a normal uterus, into which the examining finger, passed *per vaginam*, could be made to enter. There were also two omental adhesions passing down to and completing the closure of the vagina. By subsequent operative attempts the recto-vaginal fistula was closed except for one small pinpoint hole.

The second patient was admitted to hospital about the thirty-third week

of pregnancy. The foetus was felt lying more or less freely in the abdominal cavity, and in the lower abdomen a boggy mass, rather suggesting the uterus with an overlying placenta, was palpated. Four weeks later X-ray examination suggested that the foetus was nearly at term, and so the abdomen was opened. The child, which was lying free among the intestines, was delivered alive and did well. The placenta was then removed by resection of the right Fallopian tube, to which it had obtained its main attachment, and by division of another pedicle attaching it to the caecum. The mother recovered.

Dr. Wilson suggests that the findings in the first case would have been similar to those in the second if the latter had been operated upon and had not the child been forcibly pushed into the pouch of Douglas. He also suggests that if the child, in a case of full-time ectopic pregnancy, is found freely mobile in the abdominal cavity, it is because it has escaped from the amnion. And further, in such cases, the ruptured membranes, by partly ensheathing the placenta, prevent its becoming widely attached to bowel, omentum, etc., and so render removal of the placenta a simple matter.

The two cases were discussed by the PRESIDENT, Professor MUNRO KERR, and Mr. LESLIE WILLIAMS.

Professor MUNRO KERR read a paper in which he discussed certain details in the technique of the operation of lower segment Caesarean section in (*a*) clean cases, (*b*) suspect cases and infected cases, and (*c*) after failed forceps. He did not restrict the lower segment operation to patients in labour, but also employed it a week or two before term, using a more or less transverse incision. He did not advocate its use for placenta praevia, although others had obtained good results by employing it in these cases, some of them subsequently packing the uterus and lower segment. The lower segment operation was unsuitable for cases in which the foetal head was deep in the pelvis, and for contraction ring. He considered it inadvisable if the patient was to be sterilized.

With regard to the operative technique, he advised opening the abdomen in the middle line, protecting the edges of the wound and carefully packing off the intestines. He employed a transverse uterine incision in the peritoneum of the utero-vesical pouch, and a more or less transverse one in the uterus, but the latter was given a distinct upward convexity. He claimed that this lessened the risk of lateral extension of the wound, facilitated the escape of the foetal head and assisted co-aption of the uterine wound. Furthermore, on theoretical grounds a transverse incision should heal better than a vertical one.

It is in the suspect and probably infected cases that details of technique are so important. For these cases Professor Munro Kerr advised against the use of the Trendelenburg position. He advocated a long abdominal incisien with complete eventration of the uterus, careful protection of the wound and thorough shutting off of the peritoneal cavity, including packing pushed down behind the uterus, this latter pushing forward the child's head, thus helping its delivery. With regard to the removal of the placenta and membranes he recommended clamping the cord with pressure forceps, dividing the cord and then dropping the forceps into the lower segment, whence by its weight it finds its way into the vagina. The placenta is then removed

by kneading the fundus and by pressure assisted by traction on the forceps holding the cord. Before closing the uterine wound the lower segment should be disinfected, a large drainage tube should be placed in the lower segment and cervix and have its end projecting well down into the vagina. Gauze soaked in three per cent iodine in glycerine should be packed round this tube.

He discussed alternative methods of shutting off the peritoneal cavity by sewing parietal to visceral peritoneum, and advised the younger obstetricians to try modifications of this technique as well as the genuine extra-peritoneal operation by the Latzko method.

After failed forceps, Professor Munro Kerr thought that Caesarean section by any method was too great a risk to ask any parturient to undergo. He considered craniotomy the only alternative, unless, of course, the degree of pelvic deformity should preclude it. He also spoke against Caesarean section with hysterectomy and Portes's operation of marsupialization.

Finally he gave his figures for all his lower segment Caesarean sections for all indications. There was a total of 125 cases with three maternal deaths (2.5 per cent) and six foetal deaths (4.8 per cent).

The paper was discussed by the President, Mr. BLAIKLEY and Mr. T. F. TODD. The latter said that he was glad that Professor Munro Kerr had given approval to the Latzko extra-peritoneal Caesarean section, which seemed preferable to attempts to suture the uterine and parietal peritoneum.

Dr. W. M. FELDMAN read a paper on

NATURAL OR PHYSIOLOGICAL CONTRACEPTION.

He contended that the ideal artificial contraceptive has not been, and is not likely to be, discovered, but that a natural method of preventing an undesired pregnancy is available.

He did not claim to put forward any original work on the subject, but quoted others who had brought evidence to suggest that unfertilized ova do not survive longer than a few hours after their escape from their follicles. Therefore, he claimed that unless an ovum meets a spermatozoon within a few hours of ovulation conception could not occur.

He next discussed the works of various people who had endeavoured to show that spermatozoa lose their fertility after staying inside the female body for longer than a couple of days, and proceeded to maintain that ovulation in the human female occurs at or about the middle of the cycle. If all the above contentions were proved it would follow that fruitful coitus could occur only during some four days of the cycle, viz., the fifteenth day before menstruation (day of ovulation), together with two days before that day (during which time spermatozoa may still be surviving) and one day after the fifteenth, during which the ovum may occasionally survive. It is recommended that to secure greater safety, if the avoidance of pregnancy is desired, that the limits of the fertile period should be set rather wider than as above suggested—say from the nineteenth to the twelfth day before the next expected menstruation.

In the subsequent discussion considerable doubt was thrown on the safety of the method described. Mr. Clifford White said that the findings

at the pregnancy diagnosis station at Edinburgh appeared to prove that pregnancy could occur from a single coitus at any day in the menstrual cycle. Mr. A. Davis thought that it was far from proved that ovulation always occurred at the middle of the intermenstrual period and went on to suggest that the appearance of *mittelschmerz* at almost any time in the interval proved that ovulation did occur at varying dates. If this were the case the calculation of any safe period would be impossible.

A meeting of the Section was held on Friday, October 16th.

Mr. GREEN-ARMYTAGE showed a case of

METROCHYLORRHOEA

in a London girl. The discharge began in 1928, when she was six years of age. It was intermittent and was described as milk-like, with the passage of occasionally fleshy masses streaked with blood. She was treated in several London hospitals as a case of profuse leucorrhoea. At times the discharge was as much as two pints per day. It was noticed that just before, or just after, one of these attacks of chylous metrorrhoea she frequently suffered from an outbreak of cellulitis of the right buttock resembling erysipelas. During a period of very profuse discharge she was admitted into the West London Hospital under Mr. O. Addison, and transferred to the speaker's care. Under gas and oxygen the discharge was seen to be pouring from the external os uteri at the rate of a drop per minute. It was proved to be chyle by Dr. Elworthy and Dr. Archer. It was thought possible that a lymphangioma might exist in the broad ligament or somewhere in the abdomen. Laparotomy was performed in March 1934, but nothing abnormal was discovered. In June 1934 she was readmitted because of the discharge. After a free interval it became worse than ever. Under avertin further examination was made. After inspecting the cervix and collecting fresh material for culture, a uterine sound was passed. From that moment the chylorrhoea has ceased. The child was present, and it would be seen that she was healthy and strong and development was normal. The right thigh was one and a half inches greater in circumference than the left, a condition called elephantiasis nostras. Patient search in American, Continental and British literature has failed to find a record of a similar case.

Dr. PARKES WEBER suggested that this unique case should be called one of intermittent chylous metrorrhoea. He thought there was no reason why the uterine canal should be altogether exempt from the development of a lymphatic fistula, and that the cause was a developmental abnormality in the lymphatic vessels of the uterus due to obstruction higher up. He considered that this was analogous to a case of chyluria nostras, shown by Dr. H. Morley Fletcher at the Royal Society of Medicine in 1929. He hoped that as two years had passed since the chylorrhoea that the present closure would persist.

Dr. ELIZABETH HURDON reported three cases of

TUMOUR OF THE UTERUS

secondary to cystic ovarian tumours. In two of the cases the ovarian tumours were simple pseudomucinous cystadenomata, the third was a carci-

nomatous papillary serous cyst. All were admitted to the Marie Curie Hospital with a diagnosis of cancer of the uterus. Sections of the biopsy material were shown under the microscope.

Miss ALICE BLOOMFIELD showed a case of

PRIMARY CARCINOMA OF THE FALLOPIAN TUBE.

Mr. GORDON LUKER read the notes of a very interesting and rare case of

SARCOMA OF THE CERVIX UTERI

in a woman 37 years of age. The growth presented at the os uteri was very vascular and polypoid. Biopsy showed a round-cell sarcoma, and panhysterectomy was performed. In the specimen shown the growth arose from an area in the neighbourhood of the internal os uteri. The speaker then showed a specimen from a patient 26 years of age who had a tubal pregnancy associated with or caused by an ovarian cyst. The cyst was one and a half inches in diameter, and the Fallopian tube had been kinked by the presence of the ovarian cyst. He suggested that the occlusion of the tube by this kink might have been responsible for the arrested progress of the fertilized ovum.

Mr. ARNOLD WALKER reported that he had under his care a patient treated in 1934 by radium for

A SARCOMATOUS POLYP

at a well-known hospital. She has just been delivered of a full-time child. Nothing abnormal was found during pregnancy and labour was also normal. His experience during the last eight years at the Radium Centre of the London County Council was that sarcoma of the uterus in any form is extremely rare. He suggested that the criteria accepted by many pathologists to justify a diagnosis of uterine sarcoma showed marked divergence of opinion and considered that the evidence for this diagnosis required very careful investigation before condemning a patient to all that it entailed.

Mr. JAMES WYATT then introduced Dr. A. J. Jacobs, who showed a very interesting and entertaining film of the progress of Jubilee, the chimpanzee at the Zoo.

The Royal Academy of Medicine in Ireland

A meeting of the Section of Obstetrics and Gynaecology of the Royal Academy of Medicine in Ireland was held in the Royal College of Physicians on Friday, February 14th, 1936, the PRESIDENT, Dr. J. F. Cunningham, was in the chair.

The PRESIDENT showed

A SPECIMEN FROM A PATIENT IN WHOM A CARDIAC LESION CAUSED DEATH DURING LABOUR.

The patient, a primipara, aged 33 years, appeared to be normal when she came into hospital. Her lungs and heart were examined and nothing

abnormal was found. There was no albumin in the urine. After she had been in labour for 12 hours it was thought that she was in the second stage. No vaginal examination was made. After she had been 15 hours in labour the head presented at the vulva. The patient said that she could not see at all, her eyelids became very swollen and she became cyanosed. She was given chloroform and had a very easy low forceps delivery. She was only given chloroform for seven minutes. She died suddenly, and the baby was stillborn. The forceps was used because the patient was in great distress owing to the cyanosis. At the post-mortem examination the abdominal organs and the brain were found to be normal. The lungs showed adhesions and evidence of old standing pleurisy. There was moderate fatty infiltration of the heart, but the valves were normal. There was no evidence of endocardiis. The right ventricle was dilated and its walls extremely thin. There was an ante-mortem clot in the left ventricle. He had seen two cases in which a clot had appeared, but it was in the right auricle or ventricle. This was the first time he had seen a clot in the left ventricle.

Dr. BETHEL SOLOMONS said that sudden death in labour had been attributed to various causes. Obstetric shock, as a diagnosis, usually meant ignorance of the cause of death. Embolus, post-partum haemorrhage, acute cardiac dilatation and many other factors were blamed. In this case it was impossible to exclude chloroform as the cause. He still believed that chloroform was dangerous in hospital practice, whereas it was apparently safe in the hands of an experienced practitioner. The post-mortem specimen which had been shown did not solve the puzzle.

Dr. G. C. DOCKERAY said that this was a rare specimen, and reminded him of one in the College of Surgeons in which a large ball thrombus in one of the chambers of the heart had caused death. It was a good deal larger than the clot in this case, but presumably the similar mechanism had occurred in both. Most chloroform fatalities seemed to occur in patients with normal hearts, so selection of patients for chloroform would not seem to make very much difference. Many cases of so-called acute dilatation of the heart were really cases of tachycardia with, in addition, auricular fibrillation.

Dr. F. ROYLE said that this was a case which would fill many people with alarm. There was nothing which could clinically suggest death, and it was very remarkable that death should have occurred so suddenly. Death might have been due to the anaesthetic, but apparently this was not so. Nitrous oxide and oxygen was, in his opinion, the proper anaesthetic for these cases. It would be interesting to know whether in this case the chloroform had really had any effect on the heart or not.

Dr. KERRY REDDIN said that in the last two months he had known of three patients with undiagnosed congenital cardiac disease who had been sent out of maternity hospitals. He thought there was great slackness in examining the hearts of the women and the babies in the maternity hospitals, and said that neither cardiac patients nor tuberculous ones were properly examined there.

The PRESIDENT, in replying, said that the absence of any clinical symptoms when the patient first came into hospital could be explained by

the pathological report which said that she had no valvular lesion of the heart. When she became so distressed during labour it was very difficult to know why, or why she had become cyanosed. He did not think that the anaesthetic had had anything at all to do with the death of the woman, and thought the cause of death must have been that the heart went through a great strain during labour, that strain was increased towards the end of labour, and it was then that the anaesthetic was given. This death had not altered their routine of giving chloroform. Every case was examined on admission to see if there was any cardiac lesion, and if there was, this was taken into consideration when an anaesthetic was being given.

Dr. R. V. DOWSE (in the absence of Dr. Ninian Falkiner) read

NOTES ON A CASE OF TUBAL MOLE,

and showed a specimen. The patient, a woman aged 33 years, had been married seven years when she consulted Dr. Falkiner in December 1935. She had one confinement four years previously which was normal. She stated that she had bled from November 2nd to November 14th, and since then had not bled at all. She herself thought she was pregnant and came to find out if this was so. On examination Dr. Falkiner found that the uterus did not correspond with a period of 12 weeks of amenorrhoea. He thought there was a cystic ovary on the right side. Under anaesthesia he was fairly confident that the cystic mass which he felt was the Fallopian tube, not the ovary. Three months of amenorrhoea did not suggest an unruptured tubal pregnancy. The right Fallopian tube and the right ovary were removed. Twenty-four hours after the operation she had a fairly heavy menstrual period; this was followed by another on January 8th, exactly four weeks later. The ovary showed two corpora lutea at different ages.

The PRESIDENT said that this was a rather typical history of tubal mole. The tube did not rupture. Pregnancy having terminated and the foetus being dead, the patient had apparently again become pregnant, because there were corpora lutea in the ovary.

Dr. BETHEL SOLOMONS reported

A CASE OF GRAFTING OF AN OVARY FROM ONE WOMAN TO ANOTHER, IN ADDITION TO GRAFTING A PIECE OF FUNCTIONING ENDOMETRIUM FROM THE UTERUS OF ONE WOMAN INTO THE UTERUS OF ANOTHER.*

The PRESIDENT said that this was probably the first time that an operation such as was described by Dr. Solomons had ever been performed. It was extremely interesting to hear of a graft of ovary and of endometrium being made at the same time. He thought it was common to find that a graft of an ovary into the rectus muscle failed. The ovary did not live very long. The graft often gave rise to pain, and later a cystic swelling sometimes appeared in the rectus muscle. It was interesting to note that the endometrium had an effect on the ovary as well as the ovary on the endometrium. He thought it very likely that the endometrium was a

* This was the first occasion on which the report of such an operation had been published. [See pages 487–491.] Menstruation followed after years of amenorrhoea, after grafting alone and much hormonic treatment had failed.

ductless gland, and would have this effect. He wondered if it was the patient's own ovary which was now functioning, in which case the result would be likely to be more permanent. The patient's own ovary may have been stimulated by the operation, this would have an effect on the endometrium, and the endometrium in turn reacted on the ovary. It was fairly easy to graft endometrial tissue, but it was very difficult to graft ovarian tissue.

Dr. T. M. HEALY said he thought the members of the Obstetrical Section ought to be proud of a section in which work of the kind done by Dr. Solomons was produced. He suggested that Dr. Solomons should follow up this case and report later on on the behaviour of the endometrium. It would be interesting to know the degree by which the uterus was covered with endometrium in six or eight months' time, and whether it was behaving as normal endometrium did in the ordinary individual.

Dr. A. W. SPAIN said it would be interesting to know why the first graft failed. It seemed to him that it was the ovary in this case that was the important thing, and not the endometrial graft. Incompatibility between the blood of the donor and that of the patient might explain the failure of the graft on the first occasion, and its success on the second occasion. He asked if the bloods had been grouped.

Dr. G. C. DOCKERAY said that he had been working on blood agglutinins, and referred to blood groups M and N and MN. He said that these groups were of no importance in blood-transfusion, but were of importance in hereditary problems, as were also groups A and B. It has been stated that the M and N and the MN groups were not of any importance for skin grafting. He supposed that this would apply to any other type of graft.

Dr. BETHEL SOLOMONS, in reply, said he thought a graft lasted for two or three years. He did not remove the whole of the diseased ovary which was so atrophic that it appeared useless. He had removed a piece for histo-olgical investigation. He believed that the menstruation was due to the presence of the grafted ovary and the endometrium.

He would certainly follow up the history of this patient who had already had several menstrual periods. He thought that the first graft had failed because of the absence of endometrium.